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ROENTGEN THERAPY FOR BRONCHIOGENIC CARCINOMA

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In this review we propose to compare the results obtained from roentgen therapy in a group of 125 cases of proved primary bronchiogenic carcinoma with another group of 125 proved cases in which neither roentgen therapy nor any other form of therapy was employed. Considered here, a proved case will be regarded as one in which tissue from the tumor on microscopic examination has shown the presence of carcinoma.

In all cases in our study there was microscopic confirmation of the clinical diagnosis. This point is important, because we know from experience that to make a differential diagnosis between primary carcinoma of the bronchus and other types of pulmonary lesions is often difficult. Although roentgenologic examination of the thorax is of the utmost importance in the diagnosis of this condition, it is well known that considerable inaccuracy exists in precise differentiation between primary carcinoma and other lesions by this method.

All of the 250 patients to be considered in this study were examined by the same group of clinicians and roentgenologists, and the treatment was given by the same group of radiologists. Of course, many more patients than 125 have received roentgen therapy for primary carcinoma of the bronchus, but since there were only 125 patients who did not receive any roentgen therapy it was thought advisable in our study for purposes of comparison to limit the group who did receive such therapy to the same number as those who did not.

We were first desirous of determining whether or not there was any criterion which guided the clinician in his decision as to which patient should receive roentgen therapy and which should not. In general, the untreated patients were in more precarious physical condition than those for whom roentgen therapy was advised. However, it must be said that in the earlier days of our experience with primary carcinoma of the bronchus it was generally thought that roentgen therapy was of practically no value for this condition; consequently patients were dismissed once a positive diagnosis had been established, regardless of their actual physical condition.

All authorities agree that primary carcinoma of the bronchus occurs more frequently in men than in women. In our group, for every woman affected there were four men (table 1). Healthy adults in the prime of life are most often afflicted (table 2). Extremes of age may also be encountered in rare instances; one of our patients was 2½ years of age and another 80 years of age.

Many hypotheses have been advanced to account for the apparent increase in incidence of bronchiogenic carcinoma. The roles of infection, irritation and heredity all have been advocated and denied by most observers. The patients in our group were predominantly farmers, but we could not elicit any tangible etiologic factor.

Primary carcinoma of the bronchus is usually insidious in its onset, and it is often difficult to distinguish it from other forms of pulmonary disease. It may therefore be overlooked, owing to the fact that the symptoms at the onset may blend imperceptibly with the clinical symptoms that may exist as a result of other pulmonary disease. In certain instances, however, there is a history that the patient apparently enjoyed perfect health and then suffered a sudden onset of symptoms such as pulmonary hemorrhage or severe paroxysms of cough. As may be readily seen by a review of table 3, most of our patients had symptoms that dated back for several months before the patients came for examination. Nine patients gave a history of symptoms that covered a period of two years or more before a correct diagnosis was established.

From the standpoint of symptomatology there was no difference whatever so far as the clinical course was concerned between the two groups in our series (table 4). It is important to emphasize that at times primary carcinoma of the bronchus may remain silent and the presenting symptoms may be those caused by metastatic focus. It is also important to point out that negative results on roentgenologic examination of the thorax do not always rule out the possibility of an underlying carcinoma. A physical finding that should always cause one to suspect the possibility of the existence of a bronchiogenic carcinoma is the absence or diminution of breath sounds over any portion of the lung. In a number of our cases this physical finding alone led to bronchoscopic examination, with subsequent establishment of the correct diagnosis.

The sites of metastatic foci in our cases as shown by clinical or roentgenologic examination are given in table 5. It should be mentioned in this connection

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that the incidence of these signs is at variance with that given in other reports because the incidence herein given occurred among living patients.

The sites of occurrence of the bronchiogenic tumors in our cases are given in table 6. It is noteworthy that there was a rather low incidence of peripheral

TABLE 1.—*Distribution According to Sex*

Sex	Treatment Given	Treatment Not Given
Male	97	106
Female	28	19

TABLE 2.—*Distribution According to Age*

Age, Years	Treatment Given	Treatment Not Given
Less than 20	1	1
21 to 30	5	7
31 to 40	13	11
41 to 50	34	30
51 to 60	45	47
61 to 70	25	28
More than 71	2	1

tumors, such as those originating near the pleura, and those of the "Pancoast" type. This may be attributable in part to the fact that in the majority of the cases in our study the diagnosis was based on microscopic examination of tissue obtained through the bronchoscope. Thus, many cases in which the lesion was situated in the periphery of the lung and in which the diagnosis was not established until necropsy were not included in this study.

Table 7 illustrates the histologic classification of the tumors in our study. To avoid all controversy over classification we have divided them according to their obvious structure, that is, adenomatous or epitheliomatous, and have subdivided them according to their index of malignancy as determined by Broders personally. Such a classification is simple, clear, not ambiguous, and easy to use; it seems to us more advantageous than other more elaborate and perhaps more confusing classifications.

Outstanding in table 7 is the high incidence of tumors of the highest grades of malignancy. In fact, of the 250 tumors that we are considering, 212 were

TABLE 3.—*Duration of Symptoms Before Registration*

Duration	Treatment Given	Treatment Not Given
1 to 2 months	19	23
3 to 5 months	38	33
6 to 11 months	46	39
1 year	11	10
13 to 18 months	6	6
2 years	2	3
2½ years	1	..
3 years	2	..
5 years	..	1

of the most malignant type. There is, however, nothing remarkably different in regard to the distribution of tumors according to their index of malignancy whether in the treated or the untreated groups. As a matter of fact, the index of malignancy played no role whatever in deciding whether a given tumor was or was not suitable for roentgen therapy.

For the purpose of record it can be stated that there was one case of hemangio-endothelioma of the trachea. One of the eight cases of adenocarcinoma grade 1 occurred in the trachea, one in the left upper lobe and two each in the right main bronchus, the right middle lobe and the right lower lobe, respectively. As is well known, these tumors are the so-called adenomas of the bronchi about which there has been much controversy.

Considering the types of patients that we have treated with roentgen rays, it is unfair to compare the value of operative procedures with the value of roentgen therapy in cases of bronchiogenic carcinoma. Even though the indications for pneumonectomy are not always followed rigidly, the radical operation is generally reserved for patients who have a relatively small localized tumor and who present no evidence of distant metastasis or of marked physical deterioration. The indications for roentgen therapy, on the other hand, are in general that the patient is not suitable for radical operation or that he refuses it. In short, operation is generally attempted in only carefully selected cases.

In the evaluation of surgical results in a carefully selected group of suitable cases, one must not forget

TABLE 4.—*Symptoms and Signs*

Symptoms	Treatment Given	Treatment Not Given
Cough	125	119
Dyspnea	60	76
Hemoptysis	51	53
Loss of weight	20	42
Effusion	28	24
Hoarseness	8	11
Dysphagia	8	8
Cyanosis	0	4
Pain	50	56
Fever	23	23
Clubbed fingers	0	3
Neurologic alone	0	6
Neurologic with cough	0	2
Edema of face	1	3
Strangling	8	8
Abdominal	1	0

the immediate mortality of the operation, which is still high even in the hands of the most skilled operators. To be fair, however, one must admit that progress is being made in this field and that, theoretically, radical operation still offers the patient his best chance of a cure if he survives the operation. But the patient with a bronchiogenic carcinoma is in difficult straits to decide whether to assume the high surgical risk, with a chance of curing his condition, or to take roentgen therapy, with a chance of prolonging life for an indefinite period.

On the other hand, if one abandons the idea of cure as the criterion by which the value of any therapeutic method is to be judged one can allocate to roentgen therapy a place among the valuable palliative procedures, comparable perhaps to the surgical treatment of gastric or renal cancer or to the medical treatment of cardiac, hepatic and other well known degenerative diseases. Considered thus, it seems more sensible to judge the results of roentgen therapy for bronchiogenic carcinoma from the point of view of its benefit to the patient after due consideration of the expense and the wear and tear, if not the actual misery, undergone by the patient during his treatment.

In an attempt to evaluate roentgen therapy for bronchiogenic carcinoma we will present an analysis of the results which we have obtained in a group of

125 proved cases of bronchiogenic carcinoma in which treatment has been given by various roentgenologic methods (tables 8 and 9). The terms which we have employed to designate the various kinds of treatment in the tables are sufficiently well known by most radiologists to obviate further elaboration of them. However, we should like to call attention to a point of view long held by many radiologists besides ourselves, namely that less than three courses of treatment with the "massive" technic are insufficient for all but the exceptional case. Judged in this light we think that 102 of our 125 patients had entirely insufficient roentgen therapy.

There are several reasons for this state of affairs. First, many of these patients were treated in the early days when the value of roentgen therapy was regarded as hardly greater than that of any other experimental procedure. Second, the physical condition of many patients was not good enough to justify anything more than a mild, or at most a single, course of treatment. Third, the results of the first course of treatment were

TABLE 5.—*Sites of Metastasis*

Site	Treatment Given	Treatment Not Given
Other lung	1	3
Supraclavicular node	22	18
Liver	0	5
Central nervous system	3	12
Bone	3	4
Skin	1	0
Axilla	1	0

TABLE 6.—*Site of Tumor*

Site	Treatment Given	Treatment Not Given
Right main bronchus	23	26
Left main bronchus	12	21
Right upper lobe bronchus	23	20
Left upper lobe bronchus	14	8
Right middle lobe bronchus	5	3
Right lower lobe bronchus	31	29
Left lower lobe bronchus	14	15
Trachea	3	3

often too discouraging or too indefinite to warrant continuation of roentgen therapy. Fourth, the inconvenience of further treatment at the clinic owing to personal circumstances of the patient made complete treatment impossible. Fifth, there are no exact indications to be followed in either planning or administering roentgen therapy. Sixth, knowledge of the advantages of repeated courses of treatment, based on experience, was slowly acquired.

One of the important reasons why the results of roentgen therapy are not better is the poor general condition of the patients which precludes adequate treatment. That statement is proved by the high death rate that occurs within six months or less in both the treated and the untreated groups. Not only were ninety-nine patients in the terminal stages of the disease, but also of those who did receive some treatment little was accomplished because thirty-seven of them died within four months.

Three patients lived a year or more without treatment after histologic proof of the diagnosis. As a matter of fact, all three of these patients had roentgen therapy elsewhere, but we have listed them as untreated because they did not receive treatment at the clinic. At any rate, we do not know of a single patient who is known not to have had any roentgen therapy who lived more than a year after proof of his diagnosis. Such a situation shows the fallacy of a statistical analysis for "cures" and seems to indicate a fertile field in which earlier diagnosis may improve the final results.

An analysis of the results of roentgen therapy shows some interesting and, at times, paradoxical results. It

TABLE 7.—*Histologic Diagnosis*

Type of Lesion	Grade of Lesion	Treatment Given	Treatment Not Given
Squamous cell epithelioma	1	0	0
	2	1	4
	3	24	23
	4	39	30
Adenocarcinoma	1	5	3
	2	8	3
	3	18	19
	4	29	30
Effusion		1	12
Hemangio-endothelioma		0	1

does not seem that the results of technically superior treatment were consistently better. The discrepancy can be explained easily by the fact which we have mentioned before, that we are not considering all the patients who had roentgen therapy.

Twelve patients had incomplete or "placebo" treatment, and two others had roentgen therapy of moderate voltage. Rather than send these patients home untreated and in a hopeless condition, this kind of treatment was given. Not one of these patients survived for six months. All fourteen patients, who for all practical purposes were untreated, followed the course of the untreated patients.

It should be noted that the data which we are considering do not permit any conclusions regarding the merits of any technic of treatment, because not all patients who had roentgen therapy are considered herein. It so happens that most of the patients in this review were treated by the so-called massive dose technic. However, a few patients treated by the "Coutard method" are also included. We think, therefore, that the question of the best method of

TABLE 8.—*Types of Therapy Employed*

Treatment *	Cases
Placebo or incomplete first course	12
"Moderate" voltage	2
"Massive dosage" (200 kv.)	
1 course	66
2 courses	21
3 courses	5
More than 3 courses	4
(1 four courses, 1 seven courses)	
"Fractional"	
1 course (8 patients)	10
2 courses (1 patient)	
3 courses (1 patient)	
"Protracted fractional"	4
All three types	1

* Complete or sufficient treatment in twenty-three cases.

treatment had better remain unanswered for the present.

We have already given our reasons for not considering fourteen cases in the group when forming a judgment of the results of roentgen therapy for bronchiogenic carcinoma. If, now, we deduct those additional patients who, according to accepted criteria, were insufficiently treated (since they all received less

than three courses of treatment) there remain twenty-three patients who may be regarded as completely or sufficiently treated. The remaining eighty-eight patients had various degrees of incomplete treatment.

Regardless of the amount of roentgen therapy which they actually received, twenty-five of these 125 patients

TABLE 9.—*Technic of Roentgen Therapy*

Treatment	Factors	Field
Placebo		
"Moderate"	135 kilovolts 5 milliamperes 40 cm. TSD 6 mm. aluminum 28 minutes = 560 roentgens	1 field, anterior mediastinum 1 field, posterior mediastinum
"Massive"	200 kilovolts 20 milliamperes 50 cm. TSD ½ mm. cu. + 1 mm. aluminum 20 minutes = 560 roentgens	2 fields, anterior thoracic 2 fields, posterior thoracic, in cross fire
Fractional	Same as "massive" with fewer minutes per treatment, but with same total dose	Same as "massive"
Protracted fractional	200 kilovolts 20 milliamperes 50 cm. TSD Thoreaus filter 150 to 200 roentgens for a total dose of 2,000 to 3,000 roentgens per field	4 to 6 fields

lived for at least one year after treatment. Table 10 shows the data concerning these patients. It seems to indicate that, in general, adenocarcinoma grade 1 has the most favorable prognosis of all these lesions and that, as a whole, patients with adenocarcinoma do better than those with epithelioma. Fifteen of these twenty-five patients had adenocarcinoma. Of these

TABLE 10.—*Data on Twenty-Five Patients Who Lived One Year or More After Treatment*

Lesion			Patient		Duration of Symptoms Before Treatment, Months	Course of Treatment	Survival After Treatment, Months
Type	Grade	Site	Age, Years	Sex			
A	4	RLL	41	♀	16	1	146
A	2	RM	56	♂	9	1	127
A	1	RLL	30	♀	24	2	119
A	3	RLL	30	♂	4	7	64
A	3	RM	63	♂	16	1	63
A	1	RM	25	♀	8	1	50
A	3	RUL	57	♀	6	2	34
A	1	Trachea	32	♀	36	3	33
S	4	RLL	64	♂	6	1	33
A	4	RLL	64	♂	2	2	31
A	1	RM	42	♀	3	3	29
A	4	RUL	48	♂	10	4	23
S	4	RLL	54	♀	7	1	22
S	4	RLL	54	♂	11	1	21
S	3	RLL	32	♂	5	2	18
A	2	LUL	48	♀	3	2	17
S	3	RUL	41	♂	6	1	17
A	3	LLL	62	♂	9	1	16
S	3	LM	59	♂	3	1	15
S	4	RLL	51	♂	4	4	14
S	3	RUL	38	♂	2	3	13
A	4	RLL	57	♂	36	1	12
A	4	LM	19	♀	8	3	12
S	4	RUL	44	♂	6	1	12
S	3	RUL	57	♂	18	1	12

Key: A = adenocarcinoma; S = squamous cell epithelioma; RLL = right lower lobe bronchus; RM = right main bronchus; RUL = right upper lobe bronchus; LUL = left upper lobe bronchus; LLL = left lower lobe bronchus; LM = left main bronchus.

fifteen lesions four were grade 1, two were grade 2, four were grade 3 and five were grade 4. Ten of these twenty-five patients had squamous cell epithelioma. Of these ten lesions, five were grade 3 and five were grade 4.

In evaluating our results of roentgen therapy in cases of bronchiogenic carcinoma, one should keep in mind that these results were produced by methods of treatment that have no associated mortality and also that all of the 125 treated patients were beyond hope of benefit from operation. Since no patient who was not treated with roentgen rays survived for longer than a year, and since twenty-five patients who were treated lived from one to twelve years, the absolute value of roentgen therapy as a palliative measure for bronchiogenic carcinoma seems self evident.

SUMMARY

In this series of 250 cases of proved bronchiogenic carcinoma the prognosis was poor because of the advanced stage of the disease at which a correct diagnosis was made. Nevertheless our results show not only that roentgen therapy is an excellent method of palliation but also that it has produced so-called cures. We therefore think that any patient who is not in too precarious a physical condition deserves to have at least one course of roentgen therapy; otherwise his life expectancy is, at most, one year. On the other hand, twenty-five patients in our series have lived from one to twelve years after roentgen therapy. The data are inconclusive but it seems that, in general, adenocarcinoma is a more favorable type of tumor than epithelioma. The question of the best method of treating bronchiogenic carcinoma with roentgen rays had better remain unanswered for the present.

ABSTRACT OF DISCUSSION

DR. MAURICE LENZ, New York: It is generally admitted that roentgen therapy of bronchiogenic carcinoma may relieve cough, expectoration, hemoptysis and pain in the chest. It is doubtful whether this treatment prolongs life. As it is difficult to fix the date of onset of the disease, a claim of increased survival following roentgen therapy must be based on a comparison of a sufficient number of treated and untreated patients. This has been done in a thorough and unbiased analysis of 125 treated and 125 untreated patients with cancer of the lung by Drs. Leddy and Moersch. While the results are encouraging, they naturally do not compare with the results in microscopically similar tumors in more accessible locations. The authors have emphasized the fact that patients referred for roentgen therapy of bronchiogenic carcinoma usually have extensive local disease. Vigorous irradiation is not practical in such cases because of concomitant injury to large volumes of normal lung tissue which have to be included. Added to this difficulty is the danger of increased breaking down if an abscess cavity is associated with the cancer, especially if it is situated, as is frequently the case, in an atelectatic lobe. The dosage administered in bronchiogenic carcinoma is therefore much less than that proved adequate in similar carcinomas in more accessible locations. If cases were referred earlier so that only small fields would be needed to include the entire disease, larger doses could be administered and perhaps would offer more hope. I believe that the entire dose should be administered in the first and only course of treatment before retrogressive changes in the normal tissues, due to preceding irradiation, preclude the administration of adequate x-ray dosage. On the basis of autopsy and clinical records of 121 untreated and sixty-eight treated cancers of the lung, Dr. William Tenzel, my associate at Montefiore Hospital, concluded that there was a direct relationship between the length of survival and the x-ray dose estimated to reach the tumor. Thus the length of survival was raised from eleven and a half months to twenty-two months when the "estimated tumor dose" was increased from 2,000 roentgens to about 6,000. It is only by such carefully substantiated studies as set forth by Drs. Leddy and Moersch that we may hope to convince the clinician of the importance of sending earlier cases of carcinoma of the lung for roentgen therapy, and this offers the only hope for improvement in therapeutic results.

IMPROVED TECHNIC FOR REMOVAL OF SEMILUNAR CARTILAGE AND POSTOPERATIVE TREATMENT

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Fifteen years ago I was impressed with difficulties attendant on internal derangements of the knee. Principles of diagnosis were not as clearly defined as at present. Operation often resulted in many weeks or several months of disability and too often produced a joint lacking full free motion. Convalescence was frequently long and painful and the entire procedure costly. In 1927 I [1] began aspirating joints and injecting air before and after operation as a matter of routine. This experience indicated hemorrhage as probably the greatest disturbing factor. Much blood in the joint before or after operation may result in irritation, infiltration, swelling and thickening of the synovial membrane and ballooning of the joint capsule. Formation of fibrin and its absorption or organization often results in adhesions within the joint. This train of events prolongs immobility. Hence a study was undertaken with a view to keeping free blood out of the joint cavity after operation.

Arthrotomy of a normal joint can be done with a minimum of trauma, with complete hemostasis, permitting early function, a minimum period of convalescence and early return to normal activity.

PREPARATION

Problems of diagnosis will not be considered except to note that, whenever increased fluid or hydrops is present, aspiration followed by injection of air to produce moderate tension within the joint is carried out. Adequate x-ray examinations are made from whatever angle may be indicated.

The state of the joint from the standpoint of arthritis is noted. A general investigation is next carried out. Possible focal infections are searched for. Occasionally I insist that an abscessed tooth be removed or prophylaxis of the mouth performed, a sinus irrigated or a pair of tonsils removed, or a chronically infected prostate or cervix first treated.

Next a careful history is taken of wound healing, whether or not ordinary scratches or cuts heal by first intention or are prone to fester. In the latter event a patient is checked with Burky's [2] toxin for sensitivity to staphylococcus toxins and, if necessary, a course of intradermal injections of Burky's toxin is given to raise immunity.

Careful blood studies are next carried out with special reference to the cell and platelet counts, bleeding time, clotting time, clot retraction time and the prothrombin time. If there is deviation from normal in any of these, a thorough study is carried out to determine its nature, cause and correction, particularly if there is disturbance in the clotting mechanism.

Allergy to iodine, procaine hydrochloride, narcotics or the ordinary drugs which might be used is investigated.

The knee, thigh and calf are invariably scrubbed with green soap and gauze, bristle brushes being avoided; the extremity is then shaved and the area cleaned with alcohol, ether and third-strength iodine (preferably the night before operation) and swathed in sterile towels, which are removed before operation, when the skin is coated with full-strength iodine unless the patient is sensitive to it. In these rather rare cases the gentian violet solution which I introduced [3] is used.

ANESTHESIA

Local anesthesia is preferred; 3 grains (0.2 Gm.) of pentobarbital sodium is administered by mouth to adults a half hour before operation. One per cent procaine hydrochloride is used; from 20 to 40 cc. is injected into the joint after aspiration. The line of incision is next infiltrated, not more than one drop of epinephrine per ounce of solution being employed to prolong the anesthesia; a greater quantity will cause postoperative hemorrhage. Spinal anesthesia is occasionally used and rarely a general anesthesia. The more explosive types are avoided, as is the closed ether method. This precaution is necessary when the electrocautery is used.

OPERATION

The affected extremity is draped free and so arranged that it can be flexed to right angles over the side or the end of the table.

A tourniquet is never used. I agree with Aleman and Friberg [4] that it is apt to cause thrombosis in the older patients; it increases the postoperative pain, swelling and local disturbance. A tourniquet prevents hemostasis and permits postoperative intra-articular hemorrhage. Voyer [5] cautions against it for these reasons and believes that it lowers natural resistance to infection.

A short longitudinal or slightly oblique parapatellar incision is preferred but this is varied, depending on the size and structure of the knee and the associated internal derangement. In this regard, Basset's [6] book is instructive. I avoid curved or cross incisions and injury to the medial or lateral ligament and, if possible, the patella or patellar ligament. However, in elderly persons with marked osteo-arthritis the entire patella has been removed as advocated by Mader.[7]

All bleeding points are carefully clamped or coagulated by the suction tip with the high frequency electrocautery.[8] The joint is thoroughly inspected. The anterior end of the meniscus is freed with the acusector, the suction tip being held near to remove smoke and clear the view. Any bleeding points are carefully coagulated as this proceeds. The cartilage is then cut along its base, the vascular area being avoided. At first an insulated curved acusector was used but was found to be unsatisfactory. More recently the knife designed by Lowe and Breck [8] has greatly facilitated this procedure. I have had no experience with the

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Mercer [9] knife or with the use of the Leggiadro [10] knife. The entire posterior portion is removed as advised by many authors, if necessary, through posterior incision. Damage to articular surfaces is carefully avoided, as is excessive manipulation of the joint. All enlarged or disturbed portions of the subpatellar fat pad are removed. The joint is thoroughly inspected for loose bodies, synovial villi, adhesions or other pathologic disturbances as suggested by MacAusland.[11] It is then thoroughly lavaged with the procaine solution, minus epinephrine, or physiologic solution of sodium chloride, the suction being used to prevent wetting of dressings. This is a simple apparatus, 9 inches long, made of number 30 stainless steel tubing, carrying a hose connection threaded on the proximal end, with a 4½ inch insulated handle. The distal end is slightly curved over the outer 2 inches, the tip being rounded, carrying a pin-sized central opening with four similar sized openings about the circumference of the tip. A small stilet of stainless steel wire, which can be passed through the central opening, is kept at hand to clean the small holes. There is a grooved metal collar at the upper end of the insulated handle which permits contact of the electrocautery point by the assistant. This simple instrument, properly handled, greatly reduces the operative time and loss of blood, keeping the field clear. Ordinary bleeding points touched with it are momentarily dried and the current coagulates them without charring; this reduces the amount of foreign material in the wound, promotes healing and greatly reduces the possibility of infection. In the deeper regions it is most convenient; quickly applied to bleeding points, it produces hemostasis with little trouble.

A blended spark gap and tube current is preferred.[3] A good head lamp greatly facilitates the whole procedure.

Lavage with physiologic solution of sodium chloride washes up any loose bits of tissue, indicates any bleeding points, clears the wound of air-borne bacteria and prevents drying of the raw tissue surfaces.

Fingers are kept out of the wound as much as possible but, if necessary, exploration is carried out with a finger after washing the gloved hands with mercury bichloride solution. The joint is immediately afterward lavaged with physiologic solution of sodium chloride. Sponges are kept out of the wound. They are apt to leave lint within the joint, which forms minute foreign bodies. MacAusland [11] cautions against sponges.

The joint is then filled with physiologic solution of sodium chloride, which may be diluted with procaine hydrochloride; the synovium is carefully mattressed with fine black silk sutures, as are the remaining layers of tissue. The skin is closed with lock stitches of the same material. Alcohol soaked gauze is placed over the wound and covered by wrappings of sterile glazed cotton. The entire leg and posterior portion of the foot are encased in a light plaster splint or crinoline and strips of basswood, with this dressing moderately snug about the knee. Some of the joints have been closed and air injected before the dressings were applied; this or the fluid, with moderate pressure of the outer dressings, reduces the possibility of chance hemorrhage from any of the coagulated points.

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CONVALESCENCE

When local anesthesia is used, sweating, shock and loss of fluid associated with general anesthesia is avoided, likewise the break in food intake, all of which shortens convalescence and greatly reduces postoperative complications. The patient is permitted to sit up in bed the same day and is allowed up in a wheel chair on the third day with the affected leg horizontal. Many patients are permitted crutches on the fifth day. The splint is removed on the sixth or seventh day; also the stitches. The joint is then aspirated of any fluid and its character noted. From 20 to 40 cc., or a sufficient amount, of air is then injected to produce moderate pressure. Both passive and active motions are started. Increments of activity with regard to amplitude of motion and weight bearing are gradually and steadily increased. Patients who do not have complications bear almost their full weight on the twelfth day and use a cane on the fifteenth day. Many have been returned to full activity with no disability three weeks from the day of operation, with no synovial thickening or disturbance other than slight tenderness about the operative scar.

Injection of air is of great help in convalescence. If hemorrhage has occurred, a sufficiently large bore needle to remove it is employed. The joint may be lavaged with physiologic solution of sodium chloride through this needle until the fluid returns quite clear, when air is injected to act as a cushion. Fluid is not compressible while the air cushion prevents adhesions, adds to comfort [1] and permits greater and earlier mobility. Occasionally it is necessary to aspirate and inject a second time. MacAusland [11] nine years ago remarked on the stiffness of a joint resulting from hemorrhage. A number of patients treated in the manner described on postoperative aspirations have shown no abnormal amount or character of synovial fluid and invariably progressed to an early and complete recovery with no disability. Some of them have been carpenters, one of whom returned to full occupation on the eighteenth day after operation. Patients who do not have complications receive no physical therapy.

COMMENT

In this group of fifty cases no infection of a joint occurred. Two elderly women developed superficial stitch abscesses in the subcutaneous fatty tissues; since then stay sutures of silkworm gut have been employed instead. Twenty-six were uncomplicated cases with a hospital stay ranging from a minimum of three days to a maximum of seven. Total disability of eighteen days in one case ranged to three or four weeks; in others, up to a maximum of six weeks, females invariably progressing more slowly than males. Five females did not have complications. The maximum postoperative temperature in this group was 100.8 F. and was of short duration.

Three of the fifty cases were misdiagnosed and at operation found to be simple osteochondritis dissecans, one chondromalacia patellae and one a congenital malformation with a band of tissue snapping across the upper portion of the external condyle. One proved to be multiple chondromas, another osteochondromas with alcaptonuria. Still another was complicated by a cyst of the external cartilage and five with osteoarthritis; one by a loose body. There were five cases associated with fracture of the head of the tibia or of the condyles. Ages ranged from 8 to 61 years. Those

cases complicated by fracture or arthritis were much slower to recover and required physical therapy.

Three were complicated by hemorrhages due to blood dyscrasias, one of which responded immediately to vitamin K therapy. One peculiar case with a history of purpura and previous hemarthroses, with a very peculiar blood picture, did not respond to the administration of vitamin K, food changes or other vitamin therapy, except that the general appearance improved. The first case in which there was extensive postoperative hemorrhage occurred early in the series; there was profuse bleeding at operation and the knee joint filled with blood after operation and on aspiration a week later again refilled. Convalescence was slow, requiring three or four months, but the patient eventually obtained a knee with normal range of fairly smooth motion. In one case acute appendicitis developed the second day after operation and one was complicated by carcinoma of the uterus. One knee was opened following a second injury which damaged the external meniscus a year after removal of the internal meniscus. This joint was found to be free of adhesions and normal in every respect; there had been some regeneration of fibrous tissue along the base of the internal semilunar cartilage.

Three of the uncomplicated cases were investigated by arthroscopy a year or more following operation and the joints were found to be quite normal. This is in sharp contrast to six knees which have been investigated by exploratory arthrotomy a year or more following operation under tourniquet when the joints were known to have contained a fair amount of blood following operation. Synovial surfaces were found with many adhesions, with diminution of the joint space. Two were found to have tags or apron-like hypertrophied areas of synovial membrane associated with adhesions. These joints all presented varying amounts of limited motion before the second operation, and convalescence following it was prolonged and varying grades of joint disturbance persisted.

Boppe [12] reviewed the procedure of some twenty-one surgeons over the world eight years ago. At that time Porter allowed weight bearing in three days, others in seven, eight and nine, while most permitted weight bearing in from ten to fifteen days with full use by Henderson as early as seven days; but the majority of surgeons preferred about twenty days. A few cases respond well to early movement, weight bearing and activity. Age, weight, the general state of nutrition and the duration and extent of injury are all factors bearing on the rate of progress. Violent early motion may produce hemorrhage in the line of incision or within the joint, complicating recovery.

CONCLUSIONS

I believe that:

1. Local anesthesia is preferable to spinal or general anesthesia.
2. A thorough study of the patient should be carried out before operation.
3. A tourniquet should not be employed.
4. Complete hemostasis should be obtained.
5. Postoperative aspiration followed by injection of air greatly aids recovery.
6. Passive and active motion and function should be established early.

101 West Read Street.

12. Boppe, Marcel, and others: The Operative Treatment of Fractured or Displaced Semilunar Cartilage, J. Bone & Joint Surg. **14**: 229 (April) 1932.

ABSTRACT OF DISCUSSION

DR. ALAN DEFOREST SMITH, New York: Carefulness in preparing patients for operation and attention to details in the operation and postoperative care are to be commended. I have not found it necessary, however, to take many of the elaborate precautions which Dr. Bohlman uses, and I believe that they tend to make the treatment of this condition unnecessarily complicated. I have been hesitant about injecting air into knee joints as a routine procedure, because of the possibility of air emboli. Aspiration of the joint after operation in cases in which there is marked swelling, in order to remove the accumulated blood, is a useful procedure and should be practiced oftener. Hemorrhage after operation is nearly always due to incomplete hemostasis and not to a dyscrasia in the blood clotting mechanism. Operation in every case of internal derangement of the knee, no matter how strongly the symptoms and physical signs may point to a damaged meniscus, is to some degree an exploratory arthrotomy, because there are so many conditions which may complicate or simulate this lesion. I therefore feel that it is necessary to make a generous incision in order that the joint may be explored thoroughly. Dr. Bohlman agrees with the necessity for exploration but nevertheless prefers a short incision. It seems to me that exploration is facilitated by the use of a tourniquet, and I do not believe that this materially increases the likelihood of hemarthrosis after operation, if the tourniquet is removed before the incision is closed and if the bleeding points are ligated. The use of the coagulating current in accomplishing this is certainly helpful. Separate suture of the synovial membrane is in my opinion an important point in securing hemostasis. This has been mentioned by Dr. Bohlman. A number of authors support Dr. Bohlman in his contention that the entire cartilage should be removed. It has not been my practice to attempt removal of the posterior fourth or fifth of the meniscus, which ordinarily cannot be reached without a separate posterior incision, and I am quite certain that this small posterior tab has not resulted in any subsequent difficulty in these cases. Probably no harm is done by applying a splint for a period of a week after operation; I have preferred not to do this but to start motion the day after operation. In spite of what is said about the disadvantages of passive motion, I believe that if this is carried out carefully and gently for a few days until the patient can initiate active movements it helps greatly and practically always adds to his comfort as well as to the early mobility of his joint. I agree with Dr. Bohlman that early weight bearing is possible and desirable. The routine which I have outlined has been used in a large series of cases at the New York Orthopaedic Hospital, and in a follow-up study of 175 cases by Dr. Lantzounis no case of residual stiffness of a joint was found.

DR. PHILIP LEWIN, Chicago: Dr. Bohlman's recommendations were that: 1. Local anesthesia is preferable to spinal or general anesthesia. 2. A thorough study of the patient should be carried out before operation. 3. No tourniquet should be employed. 4. Complete hemostasis should be obtained. 5. Postoperative aspiration and injection of air greatly aids recovery. 6. Passive and active motion and function should be established early. I should like to ask Dr. Bohlman what an acusector is. I want to correct something he quoted from an earlier paper, that Porter was allowing weight bearing in three days. I can assure you that none of his patients were allowed to bear weight in three days. Regardless of whether Porter put in the questionnaire that he was letting them up in three days, or whether it was misquoted, the statement isn't true. I call your attention to a few random notes with regard to atrophy of the quadriceps muscle. There are two muscles in the body that atrophy when anything happens around them, whether disease occurs or especially if they are injured: one is the deltoid, the other the quadriceps extensor. They seem to begin quickly to atrophy. Let me call attention to a certain preoperative position for x-ray examination known as the Béclère-Holmblad position. One usually says to the x-ray man "We want an A. P. and a lateral." I always insist on three if the patient can be put in the third position. The Béclère-Holmblad position is one in which the patient kneels on a chair with the knee in a position of about 120 degrees of extension and the central ray is passed through

from behind. If you will do that in every case you won't miss any of these cases of osteochondritis dissecans that were mentioned in the author's paper. About preoperative exercises, I think it is important to tell the patient who is going to have an operation on his knee that he must practice using his quadriceps before the operation. There was a time when I used to give patients a typewritten slip saying "You must practice exercising your quadriceps before the operation because as soon as you wake up from the anesthesia (if it is a general anesthetic) I am going to insist that you raise your heel off the bed regardless of how much or how little pain it causes you." I tell them to tighten the knee, point the toes and raise the heel off the bed. They can do it with only one muscle and that is the quadriceps. If they are used to it before the operation and are thinking about it when going under the anesthetic, it is easy to get them to do it afterward. Postoperatively, they must elevate it whether they have a cast on or not, and if one has a compression cast on, they elevate that straight leg easier than if they have a pressure bandage on.

DR. HAROLD R. BOHLMAN, Baltimore: With regard to Dr. Smith's comment on air embolus, we feel pretty safe in this field. In none of these cases have we had embolism occur, even when we put in air immediately after operating, before we put on the dressings. The human body will tolerate a certain amount of intravenous air. Firor some years ago demonstrated that a dog could tolerate from 18 to 25 cc. of air in his venous system without great difficulty. I have had two cases of air embolism occur in gonorrheal arthritis joints, one of which I tried to distend when adhesions were present and another in which the joint space had been partially obliterated and I used too much tension. The immediate results were startling and very embarrassing to the patient and to the doctor as well, but neither resulted in a fatality. A number of these have been reported in the literature. I once suffered one bit of experience with air emboli in my veins while giving blood for a transfusion and somebody hooked up the vacuum pump in reverse. It was startling to feel the air gurgling up my brachial vessels; it raised my blood pressure and pulse rapidly but did no harm, although it gave me a bad start for a little while. With regard to Dr. Lewin's question on the acusector, that may not be a good term. I have forgotten who used it first, but I use it in association with a small knifelike instrument which has an insulated handle and is hooked up to a machine with a current of radio frequency characteristics. I refer to the Burdick machine, which I believe has a blended spark gap and tube current; for information on this, I refer you to Ward and Kelly's book on electrosurgery, which was published some eight years ago. Quadriceps atrophy I think depends a good deal on the duration of the disability before operation. In the oldest case in this series there were symptoms of twenty-five years' standing. The internal semilunar cartilage was badly chewed up and distributed about the joint, many pieces attached to the synovial membrane, as Timbrel Fisher notes loose bodies often do. This patient had a great deal of atrophy of the quadriceps muscle, but it came back surprisingly fast after a quarter of a century of disability of that knee. It was amazing to see how rapidly, without any particular help on our part, the quadriceps developed form and function.

Vitamin C.—Most animals do not get scurvy, however badly they are fed. They can make their own vitamin C, as the antiscurvy factor is called. But monkeys and guinea pigs need it like men. And when Holst and Frölich produced scurvy in guinea pigs in Norway in 1907 it soon appeared that it was due to lack of a substance needed in small amounts; and the quantities in different foods could be roughly measured in doses needed to cure a guinea pig. I was in the next room when Szent-Györgyi, a Hungarian working at Cambridge, isolated vitamin C. He was not looking for it and did not know that his crystals were the vitamin. He had tracked down and purified a substance found in various plants and concerned in oxidations inside the cells of both plants and animals, where it plays a part somewhat like that of hemoglobin in the animal body as a whole.—Haldane, J. B. S.: Science and Everyday Life, New York, Macmillan Company, 1940.

COMPENSATORY ATROPHY OF THE ADRENALS

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It is well known that following partial removal of an endocrine gland the remaining parts of the organ tend to compensate for the loss by undergoing active hypertrophy and hyperplasia. This phenomenon has been referred to descriptively as compensatory hypertrophy. The isolation of purified hormone principles made it possible to study the effect of hormone overdosage on endocrine glands, and it soon became evident that in most cases excessive treatment with a certain glandular substance resulted in the eventual atrophy of the cells which normally have the task of producing this glandular product. It is not within the scope of this communication to review the extensive relevant literature. Suffice it to mention that the thyroid gland undergoes involution under the influence of an overdose of a thyroid preparation,[1] the pancreatic islets, especially the insulin producing beta cells, involute following treatment with insulin,[2] the ovaries after administration of estrogen[3] or progesterone,[4] the testis after androgen

TABLE 1.—*The Action of Desoxycorticosterone Acetate on Adrenal Weights in the Rat*

Material Injected	Number of Rats	Sex	Length of Treatment, Days	Body Weight, Gm.	Adrenal Weight, Mg.	Significance of Adrenal Weight Change *
Oil	6	♂	10	152	39	Control
Desoxycorticosterone acetate	6	♂	10	152	20	P = <0.01
Cholesterol	6	♂	20	150	40	Control
Desoxycorticosterone acetate	6	♂	20	150	20	P = <0.01
Normal not injected	6	♂	20	159	38	Control
Normal not injected	6	♀	20	116	53	Control
Cholesterol	12	♂	20	157	39	P = 0.5
Cholesterol	12	♀	20	117	44	P = 0.1
Desoxycorticosterone	6	♂	20	159	19	P = <0.01
Desoxycorticosterone	6	♀	20	122	22	P = <0.01
Pregnandiol	5	♂	20	165	38	P = 0.8
Pregnandiol	5	♀	20	124	49	P = 0.3
Δ^5-dehydro-iso-androsterone	5	♂	20	160	36	P = 0.2
Δ^5-dehydro-iso-androsterone	5	♀	20	124	38	P = 0.01
Δ^5-pregnenol-3-one-20	5	♂	20	160	34	P = 0.4
Δ^5-pregnenol-3-one-20	5	♀	20	124	52	P = 0.1

* In all experiments reported in this paper, the significance of the apparent differences between the treated and control series was evaluated by "Student's" method for small samples (Fisher, R. A.: Statistical Methods for Research Workers, ed. 5, London, Oliver & Boyd, 1936, p. 128) and is expressed in terms of probability, estimated by graphic interpolation in Fisher's table of t. In accordance with the usual convention, differences between series cannot be accepted as significant when P is greater than 0.05. In each series the untreated animals or, in case all animals were injected, only the groups receiving oil or cholesterol were used as controls, since treatment with the latter substances proved ineffective in causing a change in the adrenal weight.

From the Department of Anatomy, McGill University Faculty of Medicine.

Owing to lack of space, this article has been abbreviated by omission of some of the illustrations. The complete article appears in the author's reprints.

Read before the Section on Pathology and Physiology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

The expenses of this work have been defrayed through a grant received from the Schering Corporation of Bloomfield, N. J. Drs. Gregory Stragnell and E. Schwenk of this corporation supplied all the steroids used in this work except the pregnandiol, which was donated by Ayerst, McKenna and Harrison through the courtesy of Dr. Stanley Cook. The photomicrographs have been prepared by Mr. K. Nielsen and the microscopic slides by Mr. C. Rasmussen.

1. Loeb, Leo; Bassett, R. B., and Friedman, H.: Proc. Soc. Exper. Biol. & Med. **28:** 209 (Dec.) 1930.

2. Muggia, Aldo: Arch. per le sc. med. **50:** 185, 1927. Miyari, S.: Mitt. d. med. Gesellsch. zu Tokyo, 1928, vol. 42, No. 7.

3. del Castillo, E. B., and Calatroni, C. J.: Rev. Soc. argent. de biol. **6:** 108, 1930. d'Amour, F. E.: J. Biol. Chem. **92:** lxxxv (June) 1931.

4. Selye, Hans; Browne, J. S. L., and Collip, J. B.: Proc. Soc. Exper. Biol. & Med. **34:** 472 (March) 1936.

therapy,[5] the parathyroids after administration of solution of parathyroid [6] and the adrenal cortex after administration of adrenal cortex extract [7] or desoxycorticosterone.[8] Even the pituitary shows degenerative changes in animals chronically treated with hypophysial extracts.[9] It appears logical to refer to this atrophy as "compensatory atrophy," since it is the exact antithesis of compensatory hypertrophy and appears to be the result of a readjustment of endogenous hormone production in an organism which is flooded with an exogenously introduced glandular preparation. In the case of the endocrine glands which stand under the regulating influence of the pituitary, it is most probable that compensatory atrophy is due to a decrease in the elaboration of the corresponding tropic hormone. This is shown by the fact that estrogens cause no atrophy in hypophysectomized animals whose ovaries are maintained by daily injections of gonadotropic substance,[10] and cortical preparations fail to cause cortical atrophy in intact rats receiving adrenotropic substance by injection.[11]

If the phenomenon of compensatory atrophy, as defined, is considered from the point of view of its clinical significance, it is evident that it could never serve to inhibit an excess production of hormone by an endocrine organ since, in order to produce atrophy of an overfunctional gland, one would have to administer a further excess of the same endocrine substance which is already present in unusually large amounts in the circulation of the patient. In such cases the possible benefit which could be derived from the inhibitory action exerted by the hormone on the overactive gland is outweighed by the damage which would be produced by aggravating the existing endocrine overdosage. Yet the endocrine treatment of diseases of hormone oversecretion would appear to be of the greatest clinical significance, since, in spite of all the progress made in the substitution therapy for hormone deficiencies, elimination of the hyperactive gland by surgical means or roentgen therapy are still the only reliable methods of coping with diseases of excess production of hormone.

In view of these considerations, an effort was made to determine whether treatment with glandular substances chemically similar to but physiologically different from those produced by a gland of internal secretion could also result in its compensatory atrophy. It was felt that if this should be the case it might open new methods of therapy, because the direct peripheral effects of the introduced substance would be different from those of the hormone elaborated by the hyperactive gland and would not necessarily aggravate the existing condition of overproduction of hormone.

The discovery that either estrogenic or androgenic substances may cause gonadal atrophy in both sexes,[12] which fact was confirmed with crystalline synthetic androgens and estrogens,[8] was an encouraging indication that at least in certain cases such a "transferred compensatory atrophy" is possible. However, in this instance the resulting atrophy is most probably due to the inhibition of gonadotropic hormone production, and since the latter is responsible for the maintenance of both ovary and testis it appeared possible that we are dealing with a rather unique example. Yet in cases of excessive estrogen production (e. g. women in the menopause), inhibition of ovarian function by androgens or progesterone (which, as was said, also causes ovarian atrophy) may prove of therapeutic significance. Another observation that may perhaps be interpreted as an example of transferred compensatory atrophy is the observation of de Fremery,[13] who found that diiodotyrosine causes the normally active thyroid glands of immature rats to assume the resting type. The fact that this inhibition is not due to a direct action on the thyroid is well shown by the fact that the "resting" thyroids of rats treated with diiodotyrosine remain so sensitive to exogenously introduced thyrotropic preparations that the author recommended animals so treated to be used for the bio-assay of thyrotropic extracts. It appears quite possible that the diiodotyrosine molecule, which differs but slightly from that of thyroxine, retains the latter's ability to cause compensatory thyroid atrophy though it loses its other physiologic actions.

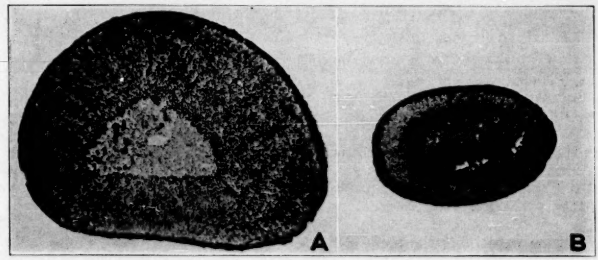

Fig. 1.—*A*, low magnification of cross section through adrenal of normal control female rat. *B*, low magnification of cross section through adrenal of female rat treated with desoxycorticosterone acetate. Note marked involution of the cortex while the medulla is but slightly subnormal in size.

In the present communication I report a series of experiments in which the compensatory atrophy of the adrenals was submitted to a systematic study. This appeared especially interesting since the adrenal produces a large number of hormone principles, many of which are available in pure crystalline form. It was thought, therefore, that this gland would furnish an excellent test object on which to study the question of whether overdosage with one hormone principle made by a certain cell could inactivate this cell sufficiently to prevent it from producing not only this but also the other hormones which it usually elaborates.

THE ACTION OF DESOXYCORTICOSTERONE

Among the investigators who studied the action of life-preserving adrenal cortex extracts on the adrenals, some claimed that these produce no significant change [14]

5. Korenchevsky, V.; Dennison, M., and Kohn-Speyer, A.: Biochem. J. **27:** 557, 1933. Schoeller, W., and Gehrke, M.: Biochem. Ztschr. **264:** 352, 1933.
6. McJunkin, F. A.; Tweedy, W. R., and Breuhaus, H. C.: Parathyroid Hormone: Its Regulatory Action on Parathyroid Glands and Toxic Effect on Tissues of Rat, Arch. Path. **14:** 649 (Nov.) 1932.
7. Ingle, D. J., and Kendall, E. C.: Science **86:** 245 (Sept. 10) 1937.
8. Selye, Hans: Canad. M. A. J. **42:** 113 (Feb.) 1940.
9. Collip, J. B.; Selye, Hans, and Thomson, D. L.: Proc. Soc. Exper. Biol. & Med. **31:** 682 (March) 1934.
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11. Ingle, D. J.; Higgins, G. M., and Kendall, E. C.: Anat. Rec. **71:** 363 (July 25) 1938. Ingle and Kendall.[7]
12. Moore, C. R., and Price, Dorothy: Am. J. Anat. **50:** 13 (March) 1932.
13. de Fremery, P.: Acta brev. Neerland. **5:** 35, 1935.
14. Lippross, O.: Endokrinologie **18:** 18, 1936. King, J. L.: Proc. Soc. Exper. Biol. & Med. **35:** 619 (Jan.) 1937.

while others observed definite involution of the cortex without any lesion in the medulla.[15] With regard to the isolated cortical steroids, Ingle and his associates [11] and Kendall [16] showed that crystalline dehydrocorticosterone and corticosterone are extremely active in causing involution of the adrenal cortex of the rat when given in daily doses of 3.3 mg. The latter investigator claimed, however, that desoxycorticosterone and its acetate differ from the aforementioned compounds in that they do not cause significant atrophy. On the other hand, Dosne and I [17] showed that slight cortical atrophy may be produced by comparatively small doses (2 mg. a day) of this compound, and larger quantities (10 mg. a day) invariably elicit severe atrophy.

There also appears to be some confusion concerning the lipoid content of the cortical cells during this compensatory atrophy. Flexner and Grollman [18] stated that the functional inactivation of the cortex is accompanied by a decrease in its lipoid content, while Dalton, Dosne and I [19] came to exactly the opposite conclusion, stating that the cortical cells of rats treated with desoxycorticosterone are especially rich in lipoid granules. Furthermore there is some contradiction regarding the sex specificity of the adrenal response. Ingle [20] stated that in the rat cortical extracts cause more pronounced involution of the adrenal cortex in males than in females. On the other hand, I,[8] who used desoxycorticosterone acetate, found the female adrenal to be more responsive, a fact which may perhaps be ascribed to the proportionately larger cortex in this sex.

Numerous investigators have studied the action of cortical steroids on the "X zone" of the mouse adrenal, which, in the opinion of some, represents the "androgenic" or male hormone secreting part of the cortex. This zone is well developed in prepuberal animals of both sexes but disappears in the male after sexual maturity is attained and reappears only in case of castration. The question of whether the life-maintaining cortical principles influence this zone as well as the rest of the cortex is of especial interest, because functionally the X zone supposedly differs from the remaining cortical tissue. Robson and Taylor [21] asserted that cortex extracts containing the life-maintaining principle elicit no change in the adrenals of the mouse. Howard [22] obtained similar negative results with desoxycorticosterone and from this she concluded that the disappearance of this zone is specific to androgens, so that one may regard it as functionally not equivalent to the permanent cortex of the adrenals. In this respect her conclusions are in contradiction to those of Gersh and Grollman,[23] who stated that cortex extracts and desoxycorticosterone acetate inhibit development of the X zone in immature animals. In view of these contradictory results, I decided to reinvestigate this problem in both the rat and the mouse. My first series consisted of a number of experiments performed on 2 to 3 month old albino rats. In every case desoxycorticosterone acetate and all other steroids were administered in daily doses of 10 mg. subcutaneously, this amount being dissolved in 0.4 cc.

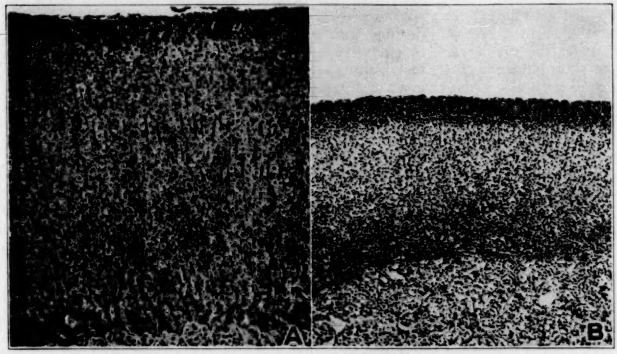

Fig. 2.—*A*, high magnification through total width of adrenal cortex of normal female rat. *B*, adrenal cortex of female rat treated with desoxycorticosterone acetate at same magnification as in *A*. Note marked atrophy of entire cortex without predilection for any particular zone.

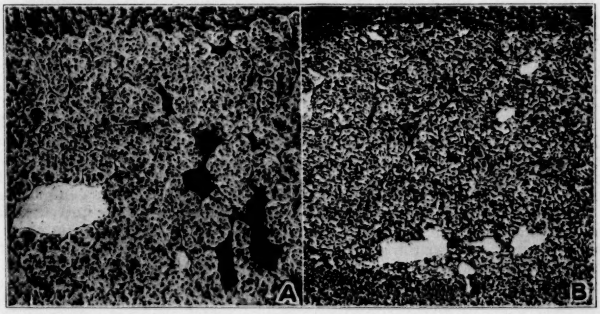

Fig. 3.—*A*, adrenal medulla of normal control female rat. *B*, adrenal medulla of female rat treated with desoxycorticosterone at same magnification as in *A*. Note shrinkage and vacuolization of medullary cells and scattered strands of dense connective tissue.

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of pure peanut oil. In all instances the melting points of the steroids were determined in order to ascertain that the samples were sufficiently purified. With the exception of the pregnenolone, a technical preparation having a melting point of 183 C. instead of from 189 to 190 C., all melting points were correct.

It appears from the results summarized in this table that desoxycorticosterone acetate has a very pronounced effect on the adrenals, whose total weight it decreases significantly in both sexes. The atrophy reaches its maximum after ten days and does not become more severe if treatment is continued for another ten days. It is also evident from table 1 that, although the females are somewhat smaller than the males in a series such as this in which all animals were of approximately the same age, the adrenals are heavier in the former. Microscopic examination shows that this difference is due almost entirely to the larger size of the cortex in the female. This explains why desoxycorticosterone causes a more pronounced loss in the weight of the female adrenal, since it decreases the amount of cortical tissue to a minimum, and in the case of the female there is more cortical tissue in which the atrophy can show itself. Thus in table 1 it will be seen that the weight of the adrenals decreased to the average of from 19 to 22 mg. in all groups treated with desoxycorticosterone acetate, irrespective of sex or length of treatment. In order to establish whether this action of desoxycorticosterone acetate is specific, a number of other sterols were tested for their adrenal activity and the table indicates that neither cholesterol nor pregnandiol or pregnenolone has any such effect, so that it seems justified to assume that this action is not merely due to the introduction of a certain amount of any steroid substance. On the other hand, Δ^5-dehydro-*iso*-androsterone caused a significant decrease in adrenal weights in the females. As this compound is an active androgen, I shall discuss this finding later, with the action of other androgens.

Microscopic examination of this material revealed that all three zones of the adrenal cortex participate approximately equally in the atrophy of the organ. In this respect the histologic structure of the cortex is very different indeed from that of a hypophysectomized animal. After ablation of the pituitary the zona reticularis is the first to undergo atrophy; in fact its degeneration is usually so rapid in the rat that numerous hemorrhages appear in this region. No such change is visible in the animals treated with desoxycorticosterone (figs. 1, 2 and 4). It is not easy to understand this difference in appearance because the most logical explanation of the mechanism responsible for this compensatory atrophy is to assume, as Ingle [24] suggests, that it is due to a decrease in the production of adrenotropic hormone. Yet if this were correct the appearance of the cortex should be the same whether the atrophy is caused by surgical removal of the anterior lobe or by hormonal inhibition of its adrenotropic hormone production. It is noteworthy that the lipoid content of the atrophic cortical cells was always very high in the rats treated with desoxycorticosterone as long as degeneration did not proceed too far.

Although the medulla showed no conspicuous decrease in size, microscopic examination indicates that it also is affected. Its cells are vacuolized and show signs of degeneration. In many instances the connective tissue stroma undergoes marked proliferation between the endocrine cell cords (figs. 3 and 5). It is conceivable that the medullary changes are merely the consequence of the decreased blood supply which reaches the adrenals as a sequel to the cortical atrophy, since most of the arterial vessels which supply the gland break up into a capillary network in the cortex before reaching the medulla. Yet in hypophysectomized animals whose cortex is likewise atrophic such medullary changes are not commonly observed. Whatever the mechanism of these medullary changes may be, they seem to represent a typical example of "transferred compensatory atrophy."

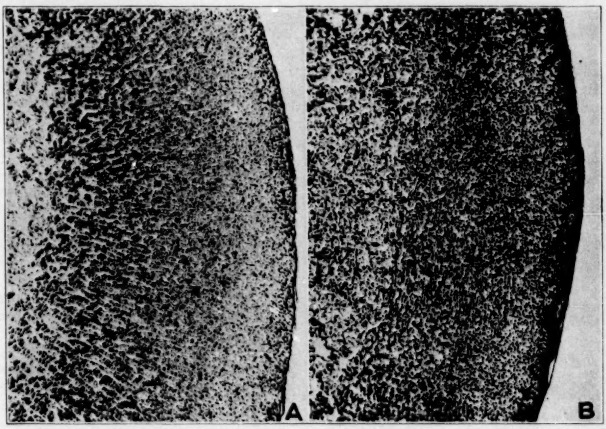

Fig. 4.—*A*, high magnification of adrenal cortex in normal control male rat. *B*, adrenal cortex of desoxycorticosterone acetate treated male rat at same magnification as in *A*. Note marked atrophy of all cortical layers.

The action of desoxycorticosterone acetate on the X zone of the mouse adrenal was studied in a group of 1 month old albino mice. In this strain the X zone is always well developed in normal females and castrates of both sexes but is absent in normal males, presumably because the presence of an active testis makes the function of this androgenic tissue unnecessary. Both desoxycorticosterone and cholesterol which was used for control purposes were administered during twenty days in daily doses of 3 mg. subcutaneously in peanut oil. The results are summarized in table 2. From this table it appears that in the mouse as in the rat the adrenals are larger in the female than in the male, and this sex difference is not completely eliminated by gonadectomy. Desoxycorticosterone acetate causes a marked reduction in the total weight of the gland in gonadectomized animals of both sexes, and microscopic examination shows that this is accompanied by com-

24. Ingle, D. J.: Am. J. Physiol. **124**: 627 (Dec.) 1938.

plete disappearance of the X zone (figs. 6 and 7 *A*). It appears therefore that this compound, which is not a testis hormone, is capable of causing involution of the presumably androgenic zone. If it should prove correct that the X zone is functionally different from the remaining cortex and is the source of adrenal androgens, one would have to consider this change to be another example of "transferred compensatory atrophy." In any case the microscopic appearance of the cortical cells was such in all zones of the organ that it seems very probable that their ability to produce hormones other than desoxycorticosterone was likewise impaired, the atrophy appearing to be "transferred" even in this respect.

TABLE 2.—*The Action of Desoxycorticosterone Acetate on Adrenal Weights in Mice*

Material Injected	Number of Mice	Sex	Body Weight, Gm.	Adrenal Weight, Mg.	Significance of Adrenal Weight Change *
Not injected	6	♂	24	3.5	—
Not injected	6	Castrate ♂	20	3.7	P = 0.6
Cholesterol	6	Castrate ♂	21	3.2	P = 0.5
Desoxycorticosterone acetate	6	Castrate ♂	21	2.7	P = 0.04
Not injected	6	♀	22	4.8	—
Not injected	6	Spayed ♀	21	4.7	P = 0.7
Cholesterol	6	Spayed ♀	23	4.4	P = 0.3
Desoxycorticosterone acetate	6	Spayed ♀	21	2.6	P = 0.03

* The significance of the apparent differences has been calculated, the noninjected castrates being used as controls for the treated castrates and the noninjected intact animals as controls for the noninjected castrates.

THE ACTION OF PROGESTERONE

Using relatively small doses (2 mg. a day) of progesterone, I [8] obtained only slight adrenal atrophy in female rats and none in males. Clausen [25] was unable to produce a statistically significant decrease in the adrenal weights in this species, but this might have been due to the fact that he used relatively small doses. In the mouse, Starkey [26] asserted, without having experimental evidence to support his assertion, that progesterone might cause involution of the X zone. This has been contradicted by Martin,[27] Tolenaar [28] and Howard,[22] who stated that progesterone in daily doses up to 5 mg. causes no change in the X zone of the adrenal in immature mice. Hence it was concluded that this hormone cannot be made responsible for the physiologic involution of this zone during gestation.

In view of the fact that the experiments mentioned in the previous section showed definitely that desoxycorticosterone causes marked adrenal atrophy, it appeared of special interest to establish whether progesterone, which differs from the latter only in the absence of one –OH group on C atom 21, would have the same effect. For this purpose 12 female albino rats weighing on the average 107 Gm. were divided into two groups of 6. The first group received only 0.4 cc. of peanut oil subcutaneously daily; the second group was injected with 10 mg. of progesterone in the same amount of oil. After twenty days of treatment, all animals were killed. The average adrenal weight in the control group was 40 mg. at this time, while in the progesterone-treated group it was only 29 mg. This decrease is obviously statistically significant since P = <0.01. Another experiment of this type was performed on 12 castrate male albino rats weighing 175 Gm. on the average. Here again 10 mg. of progesterone was administered daily in 0.4 cc. of peanut oil to one group while the other group was treated merely with peanut oil. The average adrenal weight was 40 mg. in the controls and 36 mg. in the progesterone-treated group. However, this decrease was not statistically significant since P = 0.3. The reason progesterone failed to cause more significant atrophy in this group is probably that these animals were much heavier than those of the previous group and yet received the same dose of the substance. Several other experiments in which we studied the action of progesterone confirmed these observations, as they showed that this compound causes some decrease in adrenal weight but is much less potent in this respect than desoxycorticosterone.

In 6 gonadectomized female albino mice having an average body weight of 21 Gm., daily administration of 3 mg. of progesterone caused a decrease in the average adrenal weight from 4.7 to 3.8 mg. (P = 0.05), while in 6 males of the same size the average adrenal weight of the noninjected castrates (3.7 mg.) was approximately the same as that of the progesterone-treated animals (3.9 mg.). These results confirm the view expressed in our previously quoted paper, namely that the female organism is more sensitive to this action of progesterone than the male. At the same time a comparison of the atrophy produced in these groups with the decrease in adrenal weight caused by treatment with desoxycorticosterone acetate under exactly identical conditions (see the previous section of this communication) shows beyond doubt that the slight change in the molecular structure of desoxycorticosterone which results in its transformation into progesterone greatly reduces its ability to cause adrenal atrophy.

Microscopic studies of the adrenals of progesterone-treated rats showed lesions which were essentially similar to those elicited by desoxycorticosterone but were much less pronounced. In the gonadectomized mouse, the most conspicuous result of progesterone therapy was the disappearance of the X zone in both sexes (fig. 7 *B*).

TABLE 3.—*Inhibition by Various Steroid Compounds of the Adrenal Hypertrophy Caused by Estradiol*

Material Injected	Number of Rats	Sex	Adrenal Weight, Mg.	Significance of Adrenal Weight Change *
Not injected	6	♂	35	Control
Estradiol	6	♂	48	P = <0.01
Estradiol and progesterone	6	♂	39	P = 0.08
Estradiol and testosterone	6	♂	41	P = <0.01
Estradiol and desoxycorticosterone acetate	6	♂	39	P = 0.08
Not injected	6	♀	42	Control
Estradiol	6	♀	48	P = 0.1
Estradiol and progesterone	6	♀	47	P = 0.1
Estradiol and testosterone	6	♀	43	P = 0.5
Estradiol and desoxycorticosterone acetate	6	♀	46	P = 0.7

* The statistical significance of the apparent change in adrenal weight is expressed in comparison with the noninjected normals in the case of the animals treated with estradiol alone. In all other cases the result of combined treatment with two compounds is compared with that of mere estradiol administration.

THE ACTION OF ANDROGENS

While most investigators agree that the X zone of the mouse adrenal disappears under the influence of androgens,[29] no significant change in the weight or histologic structure of the adrenal has been observed

25. Clausen, H. J.: Read before the meeting of the American Association of Anatomists, Louisville, Ky., March 20-22, 1940.
26. Starkey, W.: Univ. Pittsburgh Bull., October 1937, vol. 34.
27. Martin, S. J.: Proc. Soc. Exper. Biol. & Med. **28**: 41, 1930.
28. Tolenaar, J.: Acta brev. neerl. **9**: 54, 1939.

29. Poll, Heinrich: Deutsche med. Wchnschr. **59**: 567 (April 14) 1933; Anat. Anz. **77**: 113, 1933. Martin.[27] Howard.[22]

in lizards,[30] guinea pigs[31] and dogs.[32] Vidgoff and Vehrs[33] stated that in the rat the so-called inhibitory hormone of the testis, which causes involution of the male sex organs, leads to hypertrophy of the adrenal cortex. However, I[34] demonstrated that all nonspecific agents which cause gonadal atrophy also produce enlargement of the adrenal cortex, and therefore it appears very probable that the relatively crude testis extracts employed by Vidgoff and Vehrs owe both their adrenal enlarging and sex organ inhibiting actions to their toxicity. Crystalline testosterone causes definite adrenal atrophy in immature females[35] and a less pronounced decrease in adrenal weight in adult females,[36] but no such decrease could be obtained in adult males.[8] It is of interest that in the case of early postnatal treatment with testosterone propionate the cortical atrophy is particularly marked in the rat but is due mainly to involution of the glomerulosa.[37] In this respect the atrophy differs qualitatively from that produced by hypophysectomy, which, as I mentioned before, is characterized by a predominant reticularis atrophy.

Since the adrenals are smaller in males than in females, the fact that a definite decrease in adrenal weight was obtained only by androgens in female rats might be regarded as an indication that this change is due merely to a "masculinization" of the female. In order to test this possibility my associates and I performed an experiment in a group of 12 newborn albino male rats, 6 of which received 1 mg. of testosterone daily during twenty-four days, beginning on the day of birth. The dose was then raised to 3 mg. daily, the animals being killed on the thirtieth day of treatment. The remaining 6 rats received the same dose of cholesterol during this period and served as controls. The experiment was performed on such immature animals because previous observations taught us that it is easier to inhibit the development of the adrenal than to cause atrophy of a fully developed gland. The average adrenal weight in the controls was 24 mg. as compared with 12 mg. in the testosterone-treated group. The decrease was obviously statistically significant, since even the largest adrenal in the testosterone group was considerably smaller than the smallest of the control glands ($P = <0.01$). This experiment indicates perhaps that one is dealing not merely with a "masculinization" but with true compensatory atrophy, although it is not impossible that the gonads of such immature males produce so little—if any—androgen that the treatment may be regarded as "masculinization" of a neutral type.

Experiments on 6 castrate male and 6 spayed female 1 month old albino mice with an average body weight of 22 Gm. showed that daily administration of 3 mg. of testosterone during a period of twenty days caused no change in the average adrenal weight of the males (3.7 mg.), but in the females the average weight of the organ decreased from 4.7 to 3.8 mg. ($P = 0.06$). Microscopic examination showed that irrespective of the adrenal weight the X zone disappeared under the influence of the androgen in both sexes (fig. 8).

These results indicate that androgens have a definite effect on the adrenal cortex, a conclusion which receives further support through the observations recorded in table 1, that dehydro-*iso*-androsterone is also active in decreasing the adrenal weight of the female rat.

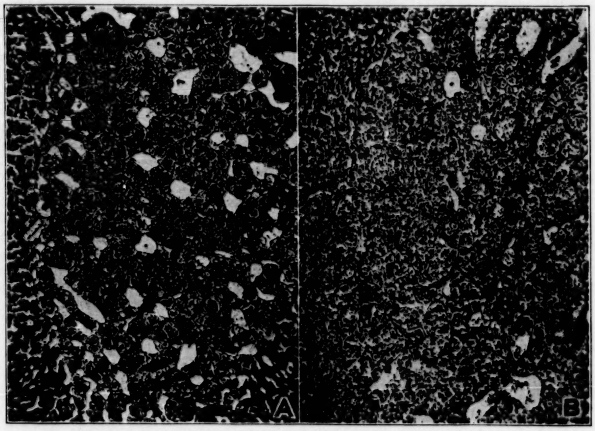

Fig. 5.—*A*, high magnification of medulla of normal control male rat. *B*, adrenal medulla of male rat treated with desoxycorticosterone acetate at same magnification as in *A*. Note marked vacuolization and involution of medullary cells.

PREVENTION OF VARIOUS TYPES OF HYPERTROPHY OF ADRENAL CORTEX BY MEANS OF STEROID HORMONES

Although early investigators who used impure preparations of estrogens obtained contradictory results,[38] Selye, Collip and Thomson[39] showed that crystalline estrone causes marked hypertrophy of the adrenal cortex in the rat, a fact which has since been confirmed for numerous other estrogens. It appeared of interest to establish whether this hypertrophy may be prevented by other steroid hormones. For this purpose a series of experiments was performed on albino rats. The average weight of the males was 154 Gm. and that of the females 109 Gm. All experimental animals were treated with daily doses of 300 micrograms of alpha-estradiol while the other steroid hormones were administered in daily doses of 2 mg. The daily dose of each of these com-

30. Forbes, T. R.: Read before the meeting of the American Association of Anatomists, Louisville, Ky., March 20-22, 1940.
31. Bottomley, A. C., and Folley, S. J.: J. Physiol. **94:** 26 (Oct. 14) 1938.
32. Nosaka, J.: Folia endocrinol japon. **12:** 26, 1936.
33. Vidgoff, Ben, and Vehrs, Herman: Endocrinology **26:** 656 (April) 1940.
34. Selye, Hans: Endocrinology **25:** 615 (Oct.) 1939.
35. McEuen, C. S.; Selye, Hans, and Collip, J. B.: Proc. Soc. Exper. Biol. & Med. **36:** 213 (March), 390 (April) 1937.
36. Korenchevsky, V.; Dennison, M., and Hall, K.: Biochem. J. **31:** 780 (May) 1937. Wolfe, J. M., and Hamilton, J. B.: Endocrinology **25:** 572 (Oct.) 1939. Mazer, Milton, and Mazer, Charles, ibid. **24:** 175 (Feb.) 1939. Selye.[8]
37. Selye, Hans: Anat. Rec. **76:** 145 (Feb. 24) 1940.
38. Watrin, J.: Compt. rend. Soc. de biol. **92:** 1451, 1925. Montpellier, J., and Chiapponi, L., ibid. **104:** 375, 1930. Shumacker, H. B., Jr., and Lamont, Austin: Proc. Soc. Exper. Biol. & Med. **32:** 1568 (June) 1935.
39. Selye, Hans; Collip, J. B., and Thomson, D. L.: Proc. Soc. Exper. Biol. & Med. **32:** 1377 (May) 1935.

pounds was injected subcutaneously in 0.1 cc. of peanut oil during a period of twenty days. The results of the experiments are summarized in table 3. The table indicates clearly that progesterone, testosterone and desoxycorticosterone are all capable of inhibiting the estradiol hypertrophy of the adrenal in males in which estradiol induced a significant cortical enlargement. In the females, the adrenals of which are larger than those of the males under normal conditions, the 300 microgram dose of estradiol used in these experiments led to no statistically significant adrenal weight increase and consequently the other steroids could not show a significant inhibition.

The fact that the adrenal enlargement normally produced by muscular exercise may be prevented by cortex extracts has been demonstrated by Ingle.[24] My associates and I [40] found that desoxycorticosterone, testosterone and progesterone may also prevent the adrenal enlargement caused by various other damaging agents such as injections of formaldehyde and surgical shock. Since during the alarm reaction elicited by such stimuli as muscular exercise, trauma or toxic doses of drugs the pituitary responds with an increase in adrenotropic hormone production [10] and the aforementioned steroids inhibit the elaboration of the adrenotropic principle by the pituitary, it is concluded that the inhibition of adrenal enlargement under these conditions is probably mediated by the hypophysis.

SUMMARY AND CONCLUSIONS

Experimental evidence indicates that both in the mouse and in the rat desoxycorticosterone actetate causes marked involution of the adrenal cortex. Histologically the atrophy of the cortical cells is very pronounced in all three zones, yet unlike the atrophy caused by hypophysectomy it is not particularly severe in the zona reticularis. Although it appears quite probable that the action of this cortical steroid is due to its ability to inhibit production of adrenotropic hormone, this observation is not easily reconcilable with such an interpretation. The cells of the adrenal medulla become vacuolized and show signs of degeneration in rats treated with desoxycorticosterone acetate.

In the gonadectomized male or female mouse the characteristic X zone of the cortex disappears under the influence of desoxycorticosterone acetate. Changes in the medulla are not readily detectable in this species.

Progesterone given in large doses also causes involution of the adrenal cortex in the rat and to a lesser degree in the mouse. This effect is evident only in females, and even in these much higher doses have to be administered to obtain an atrophy comparable to that caused by desoxycorticosterone acetate. The X zone of the mouse adrenal disappears in gonadectomized males or females treated with progesterone.

Androgens such as testosterone or Δ^5-dehydro-*iso*-androsterone are also capable of causing involution of the adrenal cortex, again much more readily in females than in males. The disappearance of the X zone, which is obtained by androgens in gonadectomized mice, is not always accompanied by a measurable decrease in adrenal weight.

Estradiol causes much more pronounced hypertrophy of the adrenal cortex in male than in female rats. This effect is inhibited by the simultaneous administration of desoxycorticosterone acetate, progesterone or testosterone.

The atrophy of an endocrine gland caused by the administration of an excess of the hormone or hormones which it produces is regarded as the exact antithesis of the compensatory hypertrophy elicited by the hormone deficiency occasioned by partial extirpation of such a gland. For this mechanism of readjustment the term "compensatory atrophy" is suggested. It is essentially the same mechanism which in human pathology is responsible for instance for atrophy of the adrenal cortex if a tumor develops in the cortex of the contralateral adrenal gland. Experimental work shows that such compensatory hypertrophy may in some instances be produced by substances other than the main product of secretion of a certain endocrine gland. Thus atrophy of the testis has been elicited with estrogens or progesterone, atrophy of the adrenal cortex with androgens or progesterone, involution of the adrenal medulla with desoxycorticosterone acetate and the like. In these cases, one is dealing with a "transferred" compensatory atrophy. This phenomenon promises to be of clinical importance, since it may afford a means by which to decrease the activity of overfunctioning endocrine glands without having to administer additional amounts of a substance which is already produced in excess. Thus, for instance, the use of desoxycorticosterone acetate (a substance which is practically devoid of androgenic activity) in cases of adrenogenital syndrome in which there is an excess production of androgen in the adrenal may prove useful in inhibiting the faulty endocrine secretion of the cortex.

40. Selye, Hans; Dosne, Christiane; Bassett, L., and Whittaker, J.: Canad. M. A. J. **43**:1 (July) 1940. Selye.[8]

ABSTRACT OF DISCUSSION

DR. J. P. SIMONDS, Chicago: Some years ago Dr. O. E. Hepler, working in our department on fat tolerance in experimental hyperthyroidism, demonstrated both anatomic and physiologic evidence of compensatory atrophy. After dogs had been fed large doses of desiccated thyroid for several weeks the thyroid gland became so small that it was often difficult to find it. When such feeding was stopped, the cholesterol of the blood rose within two weeks to the high levels characteristic of myxedema and other forms of hypothyroidism. I should like to ask Dr. Selye if he has made any observations on the permanence of this compensatory atrophy.

DR. MILTON STEINBERG, Chicago: I would mention in connection with this paper that in all probability the results were mediated through the anterior pituitary; that the results were not directly through flooding the system with the hormone but through suppressing the pituitary. I think that this work should be checked by examining the anterior pituitary microscopically and should also be checked in animals with the anterior pituitary removed; I doubt whether the effect would be present in that case.

DR. HANS SELYE, Montreal, Canada: With regard to the permanence of the lesions, I experimented only with testosterone and found that its actions are still detectable months after injections were discontinued. However, I don't believe the change would be permanent in the true sense of the word and I suppose that after a still longer period recovery would ensue. With regard to the statement that the adrenal atrophy induced by steroid hormones is indirect and mediated by the pituitary, I should like to state that this is quite in accordance with my own opinion; in fact, I have experimental evidence to prove this point. It was shown that if a hypophysectomized rat receives sufficiently large doses of adrenotropic hormone to maintain the adrenal in a normal condition, none of the steroids mentioned are able to cause cortical atrophy. This, I feel, shows distinctly that the steroids act mainly, if not entirely, by depressing the adrenotropic hormone secretion of the hypophysis. The only observation which would seem to plead against this interpretation is that the microscopic appearance of the cortex following atrophy induced by testosterone or desoxycorticosterone differs from that seen in hypophysectomized rats, a fact illustrated by the lantern slides.

MULTIPLE BENIGN CYSTIC EPITHELIOMA

REPORT OF TEN CASES IN ONE FAMILY

H. J. GOLDMAN, M.D.
ST. LOUIS

By this time the familial occurrence of multiple benign cystic epithelioma is a matter of general knowledge. As to the literature, the papers by Summerill and Hutton, by Sutton, by Beck, by Savatard and by Ricker and Schwalb supply sufficient details on the subject. A full bibliography appears in the articles by Summerill and Hutton and by Beck. The most extreme example was that of Sutton, who reported seventy-four cases in three generations. Of these, only one case was verified by biopsy; five were diagnosed by direct clinical examination and the remainder on hearsay. My own experience was made the more valuable because in seven of the ten cases a biopsy was secured—not only one specimen, but in one case three specimens and in three others two specimens. In short, twelve lesions taken from seven patients were studied. Thus it was possible to study, from one patient, a lesion from the angle of the nose, the forehead and the bridge of the nose and from another one from the lip and the scalp. This supplied an opportunity for comparison of lesions in one and the same patient as they occurred in different locations and to determine whether the processes were uniform in all the lesions.

It was a further stroke of good fortune that the family under study was a prolific one, numbering no fewer than sixteen members in the three generations affected by lesions. Moreover, the grandfather in the case had two wives, thus affording an opportunity to refer the hereditary factor to him and establish its transmission through two separate lines.

TRANSMISSION

The incidence of the condition in this family was 60 per cent. Whereas at first it was transmitted from the male to females, on subsequent occasions it was passed through the female. That is, there was not any consistent sex factor in the transmission of the disease.

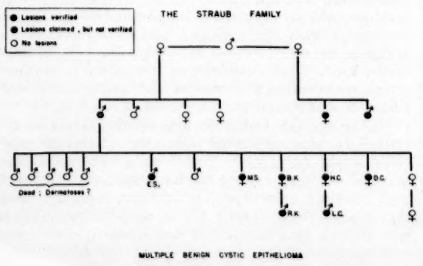

Fig. 1.—The family tree.

The ratio of males to females was 5 to 5. Most strikingly, of seven brothers and sisters in the third generation whom I was able to study, five were affected.

Read before the Section on Dermatology and Syphilology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

From the Laboratory of Dermatological Research, University of Pennsylvania School of Medicine and the Graduate Hospital of the University of Pennsylvania.

HISTORY OF CASES

Mary S., aged 30, had distribution of the lesions as illustrated in figure 2. In addition there was a solitary lesion on the left shoulder. The disease began at the time of puberty. This case has been reported in full by Weidman and Besancon.[1] The lesion from in front of the ear exhibited the microscopic appearance of tricho-epithelioma, whereas the one from the shoulder exhibited syringo-adenoma.

Elmer S. (brother of Mary S.), aged 34, has had the disease twenty-five years. The distribution is indicated in figure 3.

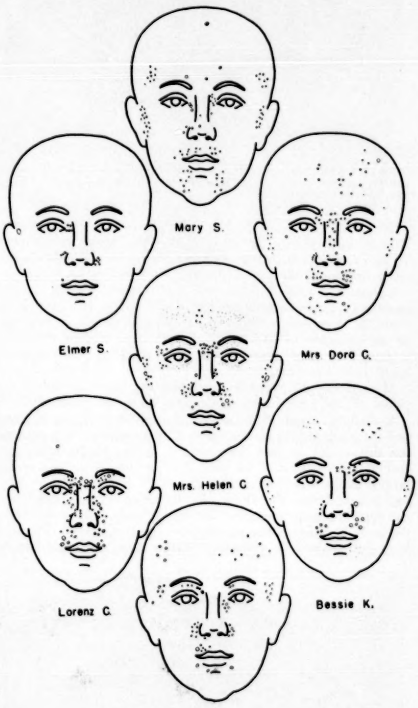

Fig. 2.—Distribution of lesions in the seven cases. Mary S. had a solitary syringo-adenoma on the left shoulder in addition. Note the large lesion on the scalp of Russell K.; there were also lesions back of the ear.

A lesion from in front of the ear exhibited the microscopic appearance of tricho-epithelioma. There were numerous large keratinous nests. The same order of process was exhibited in a lesion from the angle of the nose. Incidentally, the cells in the first lesion contained much fine granular pigment.

Mrs. Dora C., aged 32, the married sister of Mary S. and Elmer S., had onset of the condition at puberty. Three specimens of lesions were secured. In those from the angle and the bridge of the nose the picture was identical, featuring numerous keratinous nests (probably dilated hair follicles). Foreign body granulomas were also present. In the third lesion, from the forehead, the picture was essentially that of a basal cell cancer, with one exception. Thus many of the

1. Weidman, F. D., and Besancon, J. H.: Histologic Differences in a "Syringoma" of the Face and Shoulder: Employment of Wax Reconstruction, Arch. Dermat. & Syph. **21**: 279 (Feb.) 1930.

masses of cancer cells contained a smaller or larger space which was occupied by loose keratinous material. These probably represented incompletely developed hair follicles. At times the space was so small as to suggest the porelike lumen of a sweat tubule. This section is of great significance because it could scarcely be identified as tricho-epitheliomatous were it not for the evidence supplied by the other two sections.

Fig. 3.—Lesion from preauricular region of Mary S. Note the regular patterning of the lesions, i. e., comformable to positions of hair follicles and with a grouping suggestive of a hair follicle.

Mrs. Helen C., aged 39, had had the condition since puberty. The general picture of tricho-epithelioma was not clearcut. In fact, it was only the presence of a few keratinous nests which made for this suspicion. The materials were scanty.

Lorenz C., aged 9 years, the son of Mrs. Helen C., had had the condition since the age of 4 or 5 years. His hair shafts could be identified within this tricho-epithelioma in addition to the presence of two small clusters of sebaceous cells and a few keratinous nests. This was therefore unequivocally tricho-epitheliomatous.

Mrs. Bessie K., aged 44, had had the condition for thirty years. There were large numbers of keratinous nests.

Russell K., aged 15 years, the son of Mrs. Bessie K., had had the condition for eleven years. The distribution was unusual for this series in that there was a lesion on the scalp and several lesions back of the ear. The one on the scalp was the largest of the series, measuring 15 mm. in diameter and projecting 8 mm. above the surface of the skin. A specimen from the upper lip exhibited a few keratinous nests. The lesion from the scalp likewise exhibited keratinous nests and several foreign body granulomas. It differed strikingly from all the lesions in

Fig. 4.—Lesion from preauricular region of Elmer S. The general pattern of hair follicles is exhibited at the left and keratinous nests at the right.

my series in the abundance of the stroma, which was keloidal in places. This feature made it possible to recognize that the lesion was definitely set off from the surrounding tissues; that is, it was possible to recognize a definite boundary line between the lesion and its surroundings. It is noteworthy that there were no robust hairs in the lesion, as would be expected from a location such as the scalp. It is reasonable to surmise that such hairs were absent because they had remained undeveloped. It is inviting to speculate whether this lesion in the scalp indicates a sharp focalization of the original embryologic faults and too the extension of such faults to the fibrous tissues.

DISTRIBUTION OF LESIONS

The usual predilection for the angles of the nose, the inner canthi of the eyes and the corners of the mouth was exhibited in almost all the cases. By reference to the diagrams it can be observed that the region in front of the ear was strikingly affected in at least four of the cases and sparingly in two others. Apparently this position should be added to the ones already established for multiple benign cystic epithelioma. In nearly all cases there was more or less involvement of the forehead, and in one case of the scalp. The latter location should be kept in mind in future considerations of such tumors of the scalp as endothelioma. That is, in the case of tumors predominantly of the scalp, the sites of predilection for multiple benign cystic epithelioma should be examined for additional lesions and inquiries made histologically as to whether supposed cylindromas are really tricho-epitheliomatous.

ANALYSIS AND SUMMARY OF HISTOLOGIC EXAMINATION

In all twelve lesions studied [2] the epiderm was normal except for pressure atrophy such as could result

Fig. 5.—Lesion from Mrs. Bessie K. Keratinous nests dominate the picture but follicular ones can be deciphered.

from the pressure of the lesion underneath. Demodex folliculorum was not discovered at any place. Foreign body granulomas occurred in small numbers four times in three patients (Mrs. Dora C., angle of the nose and bridge of the nose; Russell K., scalp; Mary S., in front of the ear). Great numbers of fine powdery pigment grains occurred in the cells of the lesion taken from Elmer S. but not in any of the other lesions.

Features which had a bearing on the nature of the epithelial masses received particular attention, especially in the light of the hair follicle. The most unequivocal of these, namely the hair shaft, was identified with certainty only twice. In one specimen, i. e. from the upper lip of Lorenz C., it occurred in a fairly well formed hair follicle but one whose deepest parts still exhibited the features of basal cell cancer more or less. Details about a similar finding in Mary S. may be found elsewhere [1] (fig. 8). A hair papilla was also observed in the latter case. Clusters of sebaceous cells were found in close relation to the cell nests in three specimens, those of Mrs. Helen C., Lorenz C. and Mary S. These were among the strongest pieces of

2. Additional histologic considerations involving the use of these materials will be found in Traenkle, H.: The Relationship Between Epithelioma Adenoides Cysticum, Tricho-Epithelioma and Basal Cell Cancer, as Illustrated by Histologic Studies of Multiple Benign Cystic Epithelioma, Arch. Dermat. & Syph., to be published.

evidence for substantiating the diagnosis of tricho-epithelioma in the premises. Additional and less conclusive evidence consisted in the presence of epithelial strands which connected the cell nests with the surface epithelium. These were discovered in five of the twelve specimens: those of Mrs. Dora C., bridge of the nose and forehead, Elmer S., Russell K. and Mary S.

Finally, the keratinous nests, which possibly represent dilated hair follicles, were encountered consistently. They occurred in large numbers and dominated the picture in four of the specimens (those of Mrs. Dora C., angle and bridge of the nose, Elmer S. and Mrs. Bessie K.). They occurred in smaller numbers in five other specimens. In short, they were present in smaller or greater numbers in nine of the twelve specimens. With such an abundance of material it was not difficult to trace transitions between them and hair follicles; hence it may be concluded that some, if not all, of these keratinous nests represent dilated hair follicles. As they are the most consistently present, most conspicuous and most easily identified pathologic changes in the entire

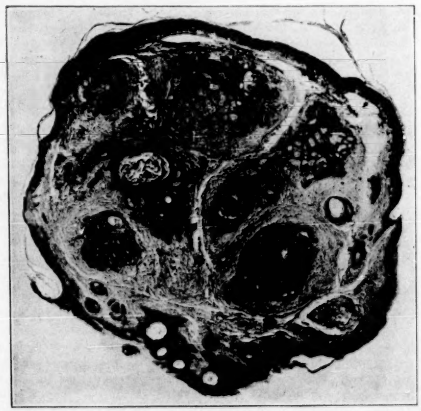

Fig. 6.—Lesion from Elmer S. Keratinous nests are small compared to the ones in figures 4 and 5, with the basal cell features now dominating the picture. Figures 6 and 7 are reduced for reproduction only half as much as figures 3, 4, 5 and 8.

series, they are the most important items in diagnosis when one is dealing with solitary cases. Accordingly, in the future the occurrence of such structures should always prompt thoughts of tricho-epithelioma whether they are connected with obvious clinical cases of multiple benign cystic epithelioma or not.

ASSOCIATION OF FORDYCE'S DISEASE OF THE MOUTH

In view of the fact that multiple benign cystic epithelioma has a distribution which suggests a role for the embryonal lines of closure of the face, four patients were examined for the presence of Fordyce's disease of the mouth. No instance was found, except that one patient had a solitary lesion of Fordyce's disease.

SUMMARY AND CONCLUSIONS

Four generations of a prolific family involving nineteen members revealed ten cases of multiple benign cystic epithelioma. Transmission took place through both male and female, and the incidence in males and females was the same. The introduction of two wives of the same male spouse at the very beginning of the family tree was particularly valuable in tracing transmission.

Seven patients were studied microscopically. As five exhibited the picture of tricho-epithelioma, it is reason-

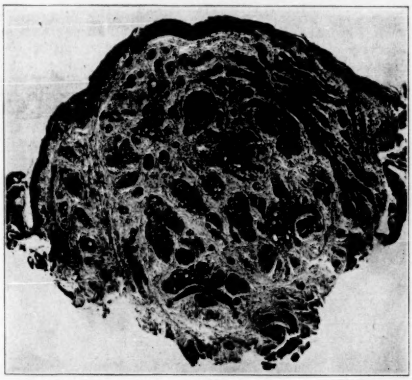

Fig. 7.—Lesion from lip of Russell K. The lesion resembles basal cell cancer, with only a few traces of keratinous nests.

able to assume that the other two were likewise tricho-epitheliomatous, at least basically. If this is a proper assumption, the picture of a basal cell cancer which cannot be recognized as tricho-epitheliomatous histologically can still make its appearance in tricho-epithelioma. If this is true for multiple benign cystic epithelioma, may it not be also true for (apparent) basal cell cancers which originate otherwise than in multiple benign cystic epithelioma; that is, in solitary lesions?

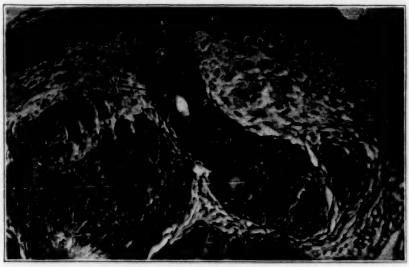

Fig. 8.—Lesion from preauricular region of Mary S. There is a hair shaft at *X*. The tissue in the sheath of its follicle is of the same character as that in the large cell nests nearby, i. e., like basal cell cancer.

The most consistently present, most conspicuous and most readily identifiable abnormality in sections was the dilatation of the hair follicle with its central keratinous nest. The appearance of keratinous nests within basal cell cancers should always provoke thoughts of tricho-epithelioma, whether seen in connection with multiple benign cystic epithelioma or not. Perhaps the pigmentation of cells in one of my cases has a similar significance,

but this point cannot be stressed because the pigmentation did not occur consistently in the sections of my series.

In addition to the commonly postulated sites of predilection for lesions, the region in front of the ear should be noted.

4500 Olive Street.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: Beginning with the discovery of one of these patients, Dr. Goldman was led to a good deal of detective work, whereby he was able to follow down the rest of the family. As a result, a rather unusual experience was met; namely, no less than 12 specimens were secured for biopsy from no less than 7 different patients. To some extent, different histologic pictures were met, and yet all of them came from the same biologic strains; that is, brothers and sisters. It seemed reasonable, therefore, to assume that all of the pathologic processes were biologically similar and, as a matter of fact, clinically they were the same entities. They were not basal cell cancers; clinically they behaved like multiple benign cystic epithelioma. That gave an excellent opportunity for reconciling and comparing the biologic with the morphologic aspects. Too much dependence cannot be placed on the microscopic appearance in appraising the biologic phenomena in the situation, which at once brings up a most practical consideration. The conclusion is, as shown by the last photomicrograph in Dr. Goldman's presentation, that a lesion which microscopically appears to be basal cell cancer is not cancer at all—at least biologically. Let me illustrate this lesson by an example. Suppose one encounters a solitary lesion clinically in which most of the microscopic picture is that of basal cell cancer. What is one going to do to determine whether the prognosis is going to be that of basal cell cancer or that of multiple benign cystic epithelioma? This is the crux; namely, that search should be made for evidence of these keratinous nests. If they are large and conspicuous, there is no difficulty at all; the matter is settled. Such nests indicate a relationship with tricho-epithelioma and from that a benign prognosis. It may be that instead of the nests being large they will be small and may have to be searched for. It may be that one would have to examine sections from different levels of the same paraffin block and perhaps it would not be a bad policy in all of our cases of basal cell cancer to examine sections from several different levels of the block in order to determine whether any of these telltale collections of keratinous material are here or there. If one finds them, the prognosis is better. If they are not found and if reasonable care has been taken to secure an examination of different levels—that is, representative positions in the same lesion—then, and then only, can one assume that the diagnosis is basal cell cancer and that therefore the less favorable prognosis must be adduced.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I agree essentially with what Dr. Weidman has emphasized. A few years ago Dr. A. E. Ingels in a case report (Epithelioma Adenoides Cysticum with Features of Syringoma, *Arch. Dermat. & Syph.* **32**:75 [July] 1935) demonstrated all types of transition between epithelioma adenoides cysticum, tricho-epithelioma and syringoma. I have seen other cases in which there were similar transitions to cylindroma. Nomland reported a case that clinically resembled multiple benign pigmented nevi but histologically was frank basal cell epithelioma. Krompecher's concept of a basal cell origin for a basal cell cancer is generally accepted. There is a predilection for involvement of the forehead and nose and inner aspects of the cheek in both malignant and benign types of basal cell epithelioma. McDonagh called attention to the fact that many mammals, especially deer, have specialized hairs in the orbital facial fold, and explained basal-cell epithelioma on the basis of the lack of need of things that are present in the lower animals, and on the basis of hereditary cell rests. Glasunow expressed the opinion that basal-cell epithelioma on the face commenced in and about the lines of fusion of the embryonic facial processes. Paljtschewsky emphasized that basal-cell growths appear in areas which are well supplied with sebaceous glands and often arise from comedones or nevi. Mallory has always championed a hair matrix origin for all types of basal-cell epithelioma. Neither in benign nor in malignant types of basal-cell epithelioma have I been able to demonstrate origin from the hair matrix cells. In the benign types, origin from the outer sheath of the outer hair follicles is frequently demonstrable and therefore one may speak of tricho-epithelioma or multiple benign cystic epithelioma. The ordinary basal cell cancer (basal cell in crypts), on the other hand, shows multiple points of origin from the basal cells of the epidermis. The same may be true in some instances of multiple benign cystic epithelioma and even is applicable to cylindromas.

DR. HERMAN GOODMAN, New York: It is conceded that the single layer of fetal ectoderm becomes the basal layer cells, which in turn, through chemical and physical changes, pass through the phases of squamous cells and corneum cells. The variations of the primary ectodermal layer become hair follicles, and so on. In facial blemishes, we have record of no less than thirty-seven supposed different types of lesions which arise from the ectodermal layer. Facial skin blemishes, for the greater part, are harmless clinically. Thousands of people receive treatment at the hands of barbers, beauticians and cosmetologists for facial skin blemishes. Rarely, if ever, is an ill effect reported. It becomes confusing, therefore, to have the terminology of skin cancer or cancer applied as a symptom or as a word in the same paragraph as epithelioma when it is utilized for benign cystic epithelioma. This presentation is the beginning of an orderly manner of continuing our studies in dermatology.

DR. DAVID BLOOM, New York: With regard to the question of heredity and family investigation, the paper by Dr. Goldman gives a hint of the value of this method. Of course, the study of one family tree in regard to a disease does not give exact information. But the study of many families with the disease and, particularly, twin studies may bring out facts which no other method of investigation has brought out until now. In dermatology there are a great number of problems which wait solution and which will probably not be solved unless newer methods of investigation are employed. I believe that cultivation of genetics in dermatology will contribute to the solution of many unsolved problems as to the etiology of disease.

DR. RICHARD L. SUTTON JR., Kansas City, Mo.: One must not be too certain of the benignancy of benign cystic epithelioma. In two cases that I have seen each of the many little tumors after having persisted for a long time in a harmless state has grown, producing a slowly progressive lesion, waxy, translucent, of hazelnut size, making a curious and typical picture. The face is grossly distorted, almost as if by nodular lepromas, with eventual ulceration. Such cases with thirty or forty progressive basal cell carcinomas at one time are difficult therapeutic problems. I have seen cases in which a lesion arching over the ear like a linear nevus, preauricular and extending upward, consisting of these little waxy pimples, took on active growth. One removes a mass of skin, including what one thinks is all of the tumor-bearing tissue; a year or two later at the upper end of the scar one removes a recurrence, and shortly one does the same thing still farther up the side of the head. Carefully questioned, practically all patients who have basal-cell carcinomas will tell, if they are observant, that the lesion began with a tiny, waxy pimple, which they thought was a blackhead and which they squeezed. Thereafter it grew. The question arises then whether their squeezing this lesion (which I presume was an epithelioma adenoides cysticum—it answers the description accurately) whether trauma changed the cell type; or did it simply translocate cells which were already potentially malignant and place them into more favorable environmental surroundings where they could grow? I think malignancy involves time considerations and that it is not possible to detect it solely by microscopic study of dead tissue. It is the prerogative only of the clinician to recognize malignant behavior, and the pathologist's original percept of whether a lesion is benign or malignant is accomplished by clinical observation. Malignancy is not a morphologic state. Many a lesion that microscopically looks

malignant isn't. Some that seem to be benign prove eventually not to be. It is only with the passage of time and as a lesion changes that one can know whether it is malignant or not.

DR. HYMAN J. GOLDMAN, St. Louis: With regard to Dr. Bloom's remarks about studying the heredity, he is right. We were inconvenienced somewhat by not being able to check up on many members of the family who could not be reached, some of them by reason of having been dead for many years. Dr. Sutton's remarks are applicable. The possibility of malignant degeneration has been discussed for many years and no definite conclusions reached. Of course, his remarks about a waxy pimple having finally turned into cancer, the waxy pimple being the description of the patient, are answered somewhat by S. Beck in his article in the Jadassohn handbook, in which he says that the only conclusive diagnosis in regard to multiple benign cystic epithelioma is the histologic one.

PRIMARY LESIONS OF THE JEJUNUM

DONOVAN C. BROWNE, M.D.
AND
GORDON McHARDY, M.D.
NEW ORLEANS

In 150,952 privately studied hospital admissions at Touro Infirmary (1926-1939) including 1,810 autopsies and 1,010,711 (1906-1939) cases at Charity Hospital of New Orleans with 6,160 (1936-1939) postmortem observations, primary pathologic changes of the jejunum were illustrated in a single instance each of traumatic regional enteritis and of intussusception, sixteen cases of diverticula, four perforated ulcers and eleven neoplastic involvements, of which seven were benign and four malignant.

This survey indicates an almost inconceivably low incidence. Yet the publications of recent years show increased cognizance of lesions of the small intestine. The number of case reports suggests either an increased incidence, the trend to report unusual pathologic conditions or diagnostic acumen. A study of the individual cases, however, reveals that only obvious lesions have been diagnosed by the clinician and roentgenologist. In many instances the establishment of the diagnosis came as a surprise to the exploring surgeon; most awaited necropsy study.

A proper concept of the anatomy and physiology of the jejunum coupled with an adequate evaluation of symptoms may increase the incidence of clinical diagnoses.

A review of reported symptomatology indicates three pertinent manifestations:

1. Pain is periumbilical or to the left and below the umbilicus, less frequently epigastric. Related to the site of the lesion it occurs at intervals after meals; the most proximal lesions cause almost immediate pain. The severity varies from quantitative discomfort in partially obstructive lesions to sharp pain when there is ulceration.

2. Obstruction is generally held to be an "all or none" phenomenon for jejunal lesions. This is inevitably so in primary intussusception and frequently so in neoplasms, especially the polypoid type, which produce intussusception in from 23 to 30 per cent of cases. This is perhaps the earliest, most frequent and most diagnostic manifestation of a jejunal neoplasm. However, jejunitis in its degrees, ulceration, diverticulosis with associated inflammation and encroaching neoplasms may produce intermittent mild and progressive blockage, depending on the mechanical nature of the pathologic condition.

3. Inanition and anemia, due to physiologic and mechanical derangement rendering nutritional absorption defective or the result of chronic blood loss, is prominent in the protracted case.

In an effort to strengthen our diagnostic armamentarium roentgenologists Pendergrass,[1] Cole,[2] Chamberlin [3] and others have made stimulating investigations on the small intestine. Reviewing radiologic failures with the present routine (fluoroscopy, immediate and six hour films) one finds the accuracy in proved instances to be less than 50 per cent for jejunal neoplasms and

Fig. 1.—Jejunal delineation with barium sulfate enteroclysis.

10 per cent for jejunal diverticula; studies are negligibly positive in primary jejunal ulcers and jejunitis. Various types and thicknesses of contrast medium have been used. Miller-Abbott [4] intubation studies and barium sulfate enteroclysis suggested by Gershon-Cohen and Shay have resulted in excellent physiologic, chemical and radiographic observations. The incidence of jejunal pathologic changes does not warrant the adoption of any of the thorough methods of roentgenologic investigation of the jejunum as a routine; this would be too costly and too time consuming. Two and four hour films taken as a routine have not proved of value. The radiologist therefore awaits the internist's alertness to request studies when indicated. When the need

Because of lack of space, this article is abbreviated in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

From the Department of Medicine, Tulane University of Louisiana School of Medicine, the Department of Gastroenterology, Touro Infirmary, and the Charity Hospital.

1. Pendergrass, E. P.: The Small Intestine, J. A. M. A. **107**: 1859-1861 (Dec. 5) 1936.
2. Cole, L. G., and Pound, R. E.: Radiology **27**: 330-338 (Sept.) 1936.
3. Chamberlain, G. W.: The Roentgen Anatomy of the Small Intestine, J. A. M. A. **113**: 1537 (Oct. 21) 1939.
4. Miller, T. G., and Abbott, W. O.: Am. J. M. Sc. **187**: 595 (May) 1934.

arises it seems likely that intubation and barium sulfate enteroclysis offer a more satisfactory mucosal delineation both as to time and as to completeness of examination, than any other method.

This presentation covers pathologic conditions which are truly primary to the jejunum, with omission of congenital defects. Bovine tuberculosis may occur primarily in the gastrointestinal tract, but necropsy studies have not shown even an isolated instance in which the jejunum was the primary site. Avitaminosis, by producing mucosal edema and motor and nerve derangement, may lead to secondary changes in the tract, producing roentgenologically distorted mucosal patterns, localized distentions and barium stagnation. Hypermotility of the small intestine is a frequent occurrence in association with instances of functional dyspepsia. Purely functional disorders, dilatation associated with migraine and other such vague entities are difficult to establish on a sound clinical basis.

INTUSSUSCEPTION

Intussusception in the jejunum represented only 0.9 per cent of 3,784 cases of intussusception reviewed by Freilich and Coe.[5] While only 5 per cent of all intussusceptions occur in adults, the jejunal type is more common to adult life than to childhood and is usually secondary to a neoplasm. Ryan and Morgan[6] reported a case which they considered primary, but there had been a previous gastro-enterostomy, which probably was related to the accident. In childhood the jejunal type is extremely rare, usually occurs without demonstrable cause and is therefore properly termed primary jejunal intussusception. In Freilich and Coe's series there were only four instances in twenty-nine cases of jejunal intussusception. The pathology of acute intussusception is the same regardless of the type and location. Clinically there are the dramatic manifestations of severely painful high intestinal obstruction. A palpable abdominal mass and bloody mucoid defecation occur in 25 per cent. Immediate surgical correction is indicated.

JEJUNITIS (REGIONAL ENTERITIS INVOLVING THE JEJUNUM)

Localized inflammatory lesions of the small intestine designated as nonspecific granulomas or inflammatory tumors have long been known. Crohn[7] reactivated interest in the entity with his 1932 publication in which he coined the term "terminal ileitis," attempting to differentiate on an anatomic basis what he then believed to be a disease state peculiar to that segment. Harris and his collaborators[8] brought recognition to enteritis at higher levels, reporting an instance in which the same pathologic process was found in the jejunum.

A study of the literature since Crohn's initial publication reveals more than 600 cases of regional ileitis but the surprising recording of only twenty instances of jejunal involvement. Wilensky[9] has ably covered the subject of etiology and was unable to ascribe the pathology to any one original cause, and he therefore concluded that it is an attempted overproductive but unsuccessful healing of a nonspecific lesion.

Through extensive studies of regional enteritis a definite correlation of the clinical manifestations with the pathologic process through four stages of the disease seems established. These studies are applicable to jejunal involvement:

1. The first phase is a state of acute inflammation with a thickened red, leathery, edematous bowel showing slight serosal exudate. The clinical picture may be that of acute appendicitis with the exception that there may be accompanying diarrhea, poor localization of pain and higher febrile rise than is expected in uncomplicated acute appendicitis. Differential diagnosis without laparotomy is not possible and its establishment as an entity is the result of careful exploration at the time of an appendectomy on a patient whose appendix does not substantiate the preoperative diagnosis of acute appendicitis.

TABLE 1.—*Thirty-Four Cases of Primary Pathologic Changes of the Jejunum*

	Touro Infirmary	Charity Hospital	Method of Diagnosis: X-Ray	Surgery	Autopsy	Symptomatology: Obstruction	Pain	Perforation	Anemia	None	Average Age	Sex: Male	Female
Admissions studied	150,052	1,010,711											
Autopsies reviewed	1,810	6,160											
Intussusception	1	0	0	0	1	1	1	0	0	0	2	0	1
Regional jejunitis	0	1	0	1	0	1	1	0	1	0	21	1	0
Ulcer	2	2	0	2	2	0	4	4	4	0	20	3	1
Diverticulum	7	9	6	0	10	2	5	1	8	8	50	5	11
Benign neoplasm	5	2	0	0	7	2	0	0	2	5	53	5	2
Malignant growth	3	1	0	3	1	3	4	0	2	0	41	3	1

We suggest conservatism at this stage, i. e. a diagnostic exploration. The pathologic process is expected to subside spontaneously. The lesion may progress to stages of chronicity, but still this premise is not adequate to indicate radical thought. The major corrective procedures (enterocolostomy, enterostomy, resection) carry a measurable risk, and recurrences in a normal segment may occur after wide resection. Time and statistics may change our present conclusions.

2. Subacute or chronic nonulcerative enteritis is a progressive state which may show periods of remission. Abdominal distress, mild diarrhea, slight febrile reactions, leukocytosis and melena have persisted. Roentgenologically there are segments showing smooth contour with uniform narrowing and spasm. This and subsequent states are surgical problems.

3. Chronic ulcerative enteritis shows additional manifestations of moderately severe anemia, obstruction and melena; there may be a palpable tumor. X-ray examination shows irregular outline and caliber, with some loss of flexibility and changes in the mucosal pattern simulating ulcerative colitis.

4. The hyperplastic stage is an advanced state of the pathologic process with apparent inanition and marked obstructive manifestations suggestive of the clinical appearance in far advanced ulcerative colitis. A radiographic study reveals obliteration of normal outlines, loss of flexibility, shortening contraction of the lumen with stenosis and occasionally fistula formation.

5. Freilich, E. B., and Coe, G. C.: Ann Surg. **105**: 183 (Feb.) 1937.
6. Ryan, T. F. J., and Morgan, W. P.: Brit. M. J. **1**: 613 (March 25) 1939.
7. Crohn, B. B.: Am. J. Digest. Dis. & Nutrition **1**: 97 (April) 1934.
8. Harris, F. I.; Bell, G. H., and Brunn, H.: Surg., Gynec. & Obst. **57**: 637 (Nov.) 1933.
9. Wilensky, A. O.: Surgery **6**: 288 (Aug.) 1939.

There is a tendency to reason in the treatment of enteritis of the jejunum as one does in that of ulcerative colitis, i. e., to reserve radical surgery for the rapidly progressive instances which do not respond to every effort at conservatism but to act before the damage is too far advanced to expect results.

Regional enteritis manifest subsequent to severe abdominal trauma has been reported by H. E. Mock [10] in three cases and by Bargen and his associates [11] at Mayo Clinic in two. In symptomatology, surgical aspects and pathology the lesions were those of regional enteritis. A single instance of such a coincidental jejunitis was encountered in our review of cases at Charity Hospital, and an abstract is included at the end of the paper.

DIVERTICULUM IN THE JEJUNUM

Diverticula in the jejunum, while still anatomic curiosities, are statistically the most prevalent primary jejunal lesions. Roentgenologically, Case [12] records the incidence to be 0.1 per cent; at autopsy instances are encountered in about 0.5 per cent of cases, according to a Johns Hopkins review. The cases are classified as congenital when the sac is made up of the same layers as the normal jejunal wall. Acquired herniations of the mucosa through the muscle layer are covered only by serosa. They are subject to inflammatory changes of diverticulitis and rarely perforate.

Etiologically they seem to be a product of degenerative changes, the greatest number being demonstrated in advancing age. The anatomic defect at the site of penetration of the blood vessels into the intestinal wall near the mesenteric attachment results in a point of decreased resistance which is subjected to irregular intestinal contractions that increase the intra-intestinal pressure. Charles Mayo [13] observed a diverticulum form, during an intestinal operation, while the proximal bowel segment was in a state of contraction. The acquired diverticulum may be due to traction of some neighboring inflammatory process, as is contended by Fletcher and Castlenden. Multiplicity is characteristic.

Jejunal diverticula are considered innocuous; careful study of 100 cases reveals related symptoms in 35 per cent. Postprandial epigastric or left hypochondriac pain, flatulence, heartburn, occasional mild obstruction and melena have been accredited to their presence. By disturbance of function of the small bowel they may produce vitaminotic and nutritional deficiencies. Diverticulitis is infrequent because of the liquid contents and the free communication between the sac and the intestinal lumen. Perforation is rare. Watson [14] reported jejunal obstruction caused by the weighty traction of an enterolith in a diverticulum.

Roentgenology offers the only prenecropsy method of diagnosis aside from surgery. Rankin and Martin,[15] in reviewing 100 surgically proved cases found an x-ray diagnosis in only 10 per cent, substantiating the contention that jejunal diverticula are more often diagnosed during operation than by radiography.

Therapeutically, surgery is the only corrective measure available. Medically, dietary restriction and measures aimed at avoidance of increased intra-intestinal pressure are offered. In the absence of clinical symptoms their removal is not justified. The severity of symptoms and the occurrence of complications indicate the need for surgical intervention. Resection, simple excision or a side tracking anastomosis are operative offerings.

CASE 1.—J. T. T., a white woman aged 69, was first seen at the age of 50 with discomfort in the lower part of the abdomen associated with constipation. Gastrointestinal studies then showed evidence of ileocecal adhesions (postappendectomy) with barium sulfate not yet in the cecum in the six hour film. When reexamined at the age of 60, free from gastrointestinal symptoms, a check gastrointestinal series showed, in addition, a single duodenal diverticulum. In 1939 she returned complaining of periumbilical pain about an hour after meals, waking her from sleep in the early morning. There were associated progressive asthenia, a slight loss of weight, anemia and mild hypovitaminosis. The patient was anemic and of small asthenic proportions, with skin and mucous membrane signs of vitamin deficiency. A radiographic study at this time revealed a single duodenal diverticulum and two diverticula in the jejunum.

Fig. 2.—Jejunal diverticulum.

A medical regimen consisting of a bland high caloric, high vitamin diet with frequent feedings and supplemental vitamins, aluminum hydroxide, sedatives and antispasmodics has not alleviated the symptoms.

This case reveals the development of diverticula in an aging patient who had a source of increased intra-intestinal pressure. The symptoms seem to be quite definitely related to the development of this pathologic picture. Operative correction seems to be the only recourse for relief, but the patient's aversion to surgery has delayed such therapy.

ULCER

Primary jejunal ulcer is a rarity. We have been able to find seventy-six reported instances since Rufz's initial publication on the subject in 1843. Apparently, this portion of the small intestine is resistant to ulceration. After gastro-enterostomy the jejunum loses its relative immunity, for marginal ulcers are frequently encountered. Our gastroscopic observations indicate that the majority of these occur in gastric mucosa at the anastomosis.

10. Mock, H. E.: Surg., Gynec. & Obst. **52**: 672-689 (March) 1931.
11. Bargen, J. A.: Wisconsin M. J. **38**: 877 (Oct.) 1939. Bargen, J. A., and Dixon, C. F.: Proc. Staff Meet., Mayo Clin. **10**: 814 (Dec. 18) 1935. Bargen, J. A.: M. Clin. North America **12**: 1573 (May) 1929.
12. Case, J. T.: Diverticula of Small Intestine, Other Than Meckel's Diverticulum, J. A. M. A. **75**: 1463 (Nov. 27) 1920.
13. Mayo, C. H.: Personal communication to J. A. Bargen, Bargen, J. A.: Rocky Mountain M. J. **36**: 537 (Aug.) 1939.
14. Watson, C. M.: Surg., Gynec. & Obst. **38**: 67 (Jan.) 1924.
15. Rankin, F. W., and Martin, W. J.: Ann. Surg. **100**: 1123 (Dec.) 1934.

In the limited study of primary jejunal lesions the etiology is even more obscure than in gastroduodenal ulceration. Theoretically, dystopic rests of the gastric mucosa may exist. The alkalinity of the jejunum is significant; gastric acidity could hardly be a factor in the development of an ulcer beyond the ligament of Treitz. Distant foci of infection, syphilis, tuberculosis, vasomotor phenomena and precedent jejunitis have an established position in the etiologic consideration. "Inherent predisposition" seems to have a place here as in the relation to the incidence of gastric and duodenal ulcers and leaves one with the conclusion that the cause of primary jejunal ulcer is unknown.

Pathologically the ulcer is a circular lesion varying from 4 mm. to 2 cm. in diameter; only 15 per cent are annular. Thickening, induration, stenosis and chronicity are prominent. The proximal portion of the jejunum is the portion of predilection, 72 per cent occupying such a site. All occur opposite the mesenteric attachment. A single ulcer is encountered in 80 per cent of cases, multiple ulcers are present in 18 per cent and associated gastric or duodenal lesions are expected in only 2 per cent. Some degree of penetration is usually present; in 82 per cent of the cases there was actual

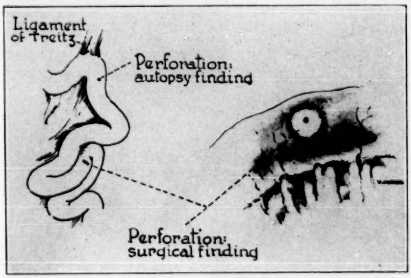

Fig. 3.—Jejunal ulcer.

perforation. Hemorrhage is recorded in 23 per cent of the cases and in all but six of these perforation also occurred. Microscopic examination revealed changes of chronic inflammation; no instance of malignant change was proved.

There is no clinical picture. Vague dyspeptic symptoms may bear slight resemblance to the "duodenal ulcer syndrome." Pain around the umbilicus or in the lower part of the abdomen is expected. If melena occurs one might expect the stool to be a cherry red. As with other pathologic changes in the small bowel, degrees of inanition and hypovitaminosis are prominent. Because of the fluid consistency of the jejunal contents, obstructive manifestations are not expected unless there is marked stenosis. Perforation results in an acute condition of the abdomen without specific localization.

Diagnosis is possible if the patient is available for radiographic study and there is sufficient suspicion to indicate delineation of the small bowel. A niche on the antemesenteric border of the jejunum with stasis proximal to the lesion is significant. A presurgical or antemortem diagnosis cannot otherwise be established.

Because of a statistical mortality of 60 per cent and the tendency to perforation, surgical intervention is the only logical therapy. There is no rationale for conservatism. Simple plication or radical resection is a matter of surgical judgment at the time of exploration.

CASE 2.—J. I., a white youth aged 19, was admitted, Nov. 23, 1939, with an acute condition within the abdomen of four days' duration. Five months previously he had attacks of colicky pain in the left inguinal region and mild postprandial discomfort in the upper part of the abdomen. An ambulatory regimen for ulcer gave no relief. In a three month interval he lost 25 pounds (11.3 Kg.). Two months prior to admission he experienced a three day period of diarrhea, profound weakness, umbilical pain and cherry red stools. This time his physician ordered a bed rest regimen for ulcer. From this time on he suffered almost constant pain in the left lower quadrant and had repeated episodes of emesis.

Four days before admission he experienced sudden severe pain in the left midsection of the abdomen which radiated to become periumbilical and later localized in the appendical area. There were associated emesis, a sharp febrile rise and a tendency to loose stools with progressive abdominal distention.

When examined the patient was acutely ill and febrile. The abdomen was distended symmetrically. There was acute tenderness in the right lower quadrant with poorly localized marked rigidity. One gained the impression of a thick edematous parietal peritoneum. No mass could be felt.

The leukocyte count was 22,000 with 93 per cent neutrophils. Flat and upright films of the abdomen were negative.

On the basis of these observations a diagnosis of a perforated hollow viscus was made, probably Meckel's diverticulum or appendix. The surgical consultant felt that the duration of the symptoms might well fit abdominal tuberculosis or Hodgkin's disease and advocated further observation.

The patient was treated conservatively with transfusions, Wangensteen suction, parenteral fluids, vitamins and alcohol. The Wassermann reaction, tests for agglutination and blood and stool cultures were repeatedly negative. Gastric analysis showed 21 units of free hydrochloric acid. The patient's condition became progressively worse with inanition and hypoproteinemia (serum proteins totaled 4.25 mg. per hundred cubic centimeters). Later he exhibited definite ileus despite from five to seven watery stools daily. Confirmatory x-ray examination also revealed free air and fluid intraperitoneally. Exploratory laparotomy revealed a perforated jejunal ulcer 24 inches beyond the ligament of Treitz. This was plicated.

On the second postoperative day pulmonary and renal infarcts developed and the patient died.

Autopsy revealed, in addition to generalized peritonitis, pulmonary and renal infarcts and the sutured jejunal ulcer another perforated jejunal ulcer 3 inches beyond the ligament of Treitz, which was oblong and measured 2 by 1 cm. Microscopic sections revealed only chronic inflammatory changes.

We cannot elicit any etiologic hint from this study. It is well illustrated that in this case a conservative medical regimen for ulcer was of no benefit. Earlier surgical intervention might have been of value.

NEOPLASM

Neoplasms primarily involving the jejunum are not as infrequently encountered as is generally thought. The actual number of cases diagnosed cannot be accurately determined, since tumors of the three divisions of the small intestine are summarily dealt with in autopsy and operative statistics. We reviewed 485 malignant and 170 benign lesions of the jejunum.

These new growths may be benign or malignant. It is confusing that carcinoids fall under both classifications. Their relative incidence is indicated by Raiford's [16] investigation of 11,000 autopsies and 45,000 surgical specimens revealing eighty-eight tumors of the small bowel, of which fifty were benign and thirty-eight malignant. Our statistical study, however, shows that malignant lesions were more frequent than the benign type. Adenoma is the commonest benign tumor, carcinoma the most frequently encountered malignant growth.

16. Raiford, T. S.: Radiology **16**: 253 (Feb.) 1931; Am. J. Cancer **18**: 803 (Aug.) 1933; Arch. Surg. **25**: 122 (July) 1932.

Etiologically it is postulated that the fluid alkaline contents with the absence of stasis explains the infrequency of malignant growths. There is no report of a chronic ulcer undergoing neoplastic change. That changes in Brunner's glands and in aberrant gastric and pancreatic tissue are etiologic factors is insignificant and, further, lacks substantiation.

Predilection does not favor the jejunum in the occurrence of neoplasms of the small bowel. An analysis of

TABLE 2.—*Malignant Tumors (485 Cases Reviewed)*

Carcinoma		234
Sarcoma	A. Lymphosarcoma	69
	B. Leiomyosarcoma	42
	C. Fibrosarcoma	20
	D. Neurofibrosarcoma	8
	E. Melanosarcoma	3
Malignant carcinoid		6
Chorionepithelioma		2
Malignant lymphoma		1

134 cases shows the duodenum predominating with fifty-one, the ileum next with forty-four and the jejunum next with thirty-nine instances.

The clinical picture is essentially the same for all neoplasms. Their differentiation is solely on a histologic basis. Flatulence, malaise, postprandial pain relieved by vomiting, asthenia and loss of weight and progressive anemia are the indefinite manifestations which occur in various degrees and combinations to precede obstruction which may be partial, recurrent, progressive or acutely complete. In adult life a neoplasm of the small bowel is the most frequent cause of intussusception. Each type of lesion has been reported as a cause, the polypoid type, of course, being the more frequent offender.

The nonoperative establishment of a jejunal neoplasm is difficult. Typical radiographic signs would be (1) dilatation of the proximal portion of the bowel with abnormal barium sulfate retention, (2) jejunal filling defect, (3) point of intestinal obstruction, (4) a dense shadow.

Surgical resection is the only curative method of management, whether the lesion is benign or malignant, for the former are certainly malignant by position and potentiality. When resection is not possible a short circuiting entero-enterostomy is the only alternative. High voltage roentgen therapy has a position of doubtful value.

Carcinoma primary to the jejunum is well established in 234 instances appearing in the literature. The relative incidence is illustrated by eight jejunal carcinomas reported from the Mayo Clinic as compared to 2,513 gastric and 2,767 rectal involvements.

The most common carcinomatous lesion is a polypoid stenosing type in favor over the annular ulcerating growths 3:1. The intestinal wall is not deeply involved until late, so that perforation is rare. It is significant that metastases are found in only 35 per cent of cases at the time of operation.

Sarcoma occurs in the small intestine more frequently than in the large bowel segments by a ratio of 2:1, as shown in Ullman and Abeshouse's [17] review. The ileum is supposedly more often involved than the jejunum because of the greater amount of lymphoid tissue in this segment. Aneurysmal dilatation is a prominent occurrence related to either muscularis infiltration or to nerve plexus destruction. Sarcomatous lesions include lymphosarcoma, leiomyosarcoma, fibrosarcoma, neurofibrosarcoma and melanosarcoma in relative frequency as listed.

Lymphosarcoma of the jejunum was found in sixty-nine cases. Starting in the lymphoid follicles, the wall is infiltrated, ulceration is characteristic and perforation results in 14 per cent of cases. Stenosis is rare, not occurring unless there is a considerable resultant fibrosis.

Leiomyosarcomas form a group of forty-two reported instances. They occur as circumscribed projecting oval tumors in half the cases and as an infiltrating mass in the other half. Showing a tendency to grow outward to the mesentery, they seldom cause obstruction.

Fibrosarcomas in twenty reports were either circumscribed or bulging with central necrosis and ulceration. As the entire wall is involved, stenosis is frequent.

Neurofibrosarcoma occurring as a primary jejunal lesion in eight cases presented no characteristic manifestation.

Melanosarcoma has been reported in three instances of jejunal involvement.

Malignant carcinoids or argentaffin tumors in the jejunum consist of nine instances found in 238 cases of involvement of the small bowel reported since Aberndorfer in 1907 differentiated these neoplasms from carcinoma. Their benignancy stressed by Forbus is disproved by more recent studies revealing metastases in 25 per cent of cases. Occurring as small submucosal nodules, they may bulge into the lumen as polypoid projections or may assume an annular form with fibrotic reaction.

Soresi [18] and Sears [19] each reported an instance of primary chorionepithelioma.

Cabot case 25242 [20] was a malignant lymphoma of the jejunum.

Benignancy of jejunal lesions is only a histologic state and as such, aside from lipomas and enterocysts, is probably only a temporary condition. The occurrence of lipomas and enterocysts in the jejunum represents 25 per cent of benign tumors of the small bowel. Table 3 shows the relative frequency of benign tumors in 170 cases.

Variations between tumor types have been classified under the most closely related cell derivation. Multiplicity is common for hemangiomas and carcinoids; the other benign tumors more commonly occur singly. Their derivation is histologically apparent except for the enterocysts. Enterocysts may be the result of

TABLE 3.—*Benign Tumors (170 Cases Reviewed)*

Tumor	Cases	Tumor	Cases
Adenoma	75	Carcinoids	15
Fibroma *	61	Lipoma	12
Myoma	33	Enterocysts	10
Hemangioma †	16	Embryonic rests	3

* Variations between myoma and fibroma are classified under the latter.
† Endotheliomas have been included under hemangiomas.

pinched off diverticula or detached epithelium from the embryonic intestine. They consist of an epithelial mucosa, a thin connective tissue submucosa and a muscularis of two layers. The content is a pale clear albuminous alkaline fluid. Occurring in the submucosa, muscularis, subperitoneal region and mesentery, they may occasion volvulus, intussusception and stenosis.

17. Ullman, Alfred, and Abeshouse, B. S.: Ann. Surg. **95**: 878 (June) 1932.

18. Soresi, A. L.: Am. J. Cancer **28**: 583 (Nov.) 1936.
19. Sears, J. B.: Ann. Surg. **97**: 110 (June) 1933.
20. Cabot Case 25242, New England J. Med. **220**: 1008 (June 22) 1939.

Enucleation, resection, marsupialization and evacuation have been employed in their management, with the former two claiming more rationale.

CASE 3.—W. A. I., a white man aged 69, first seen Jan. 3, 1940, complained of postprandial periumbilical pain spontaneously relieved within a half hour. There were three occasions of emesis. He had lost 15 pounds (6.8 Kg.). A diagnostic survey, although not positive, suggested a lesion in the upper part of the gastrointestinal tract, and exploratory laparotomy was advised. The patient refused and was not seen again until March 16. In the interval he lost an additional 21 pounds (9.5 Kg.), and an exploratory examination was again advised. On the day of hospitalization the patient experienced melena for the first time.

Examination revealed evidence of inanition. There was a questionable movable mass in the left upper quadrant.

Gastric analysis showed hyperchlorhydria. There was marked hypochromic anemia and mild hypoproteinemia. Stools showed occult blood.

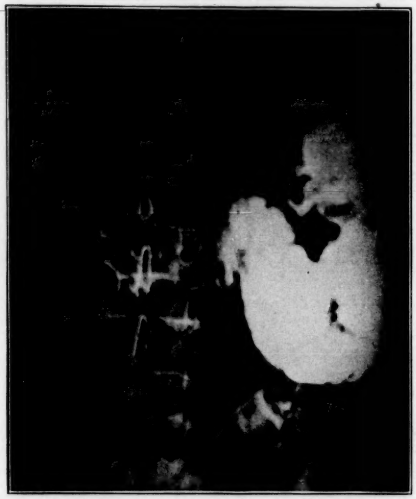

Fig. 4.—Jejunal lymphosarcoma (courtesy of Dr. Jerome Levy).

X-ray examination of the gastrointestinal tract revealed a wide sweeping curve of the duodenum with dilatation of the duodenum and proximal portion of the jejunum, barium sulfate retention and jejunal ulceration.

After adequate preparation an exploratory laparotomy was done revealing the proximal 30 cm. of jejunum enlarged and thickened, followed by an area of marked thinning studded with multiple nodules and perforated at one site. Jejunal resection, pyloric occlusion and gastrojejunostomy were successfully done.[21]

COMMENT

We present this review to bring attention to the importance of pathologic changes of the small bowel. Concentration of our study to the jejunum was stimulated by the fact that it is least often considered in a gastrointestinal survey. In our thirty-four case reports there is an indication that the more thorough study accorded the private patient increases the incidence in the private group.

21. Dr. Jerome Levy gave the authors permission to report his case illustrating a primary lymphosarcoma.

CONCLUSIONS

1. Primary pathologic lesions of the jejunum are relatively rare in contrast with other gastrointestinal lesions.

2. Clinical and roentgenologic diagnoses are infrequent; surgery and necropsy have revealed most of the instances that have been recorded.

3. Diagnosis is available by special radiographic technic, preferably enteroclysis, but such is not a practical routine procedure.

4. The clinician must become sufficiently aware of the entity to suspect its presence and request diagnostic x-ray examination.

ADDITIONAL ABSTRACTS OF CASES

JEJUNITIS

CASE 4.—A Negro youth aged 21 seven days subsequent to severe abdominal trauma experienced umbilical and left lower quadrant cramping pain followed by quantitative dyspepsia and a severe sharp pain relieved by vomiting. There was mild diarrhea, melena and low grade fever. X-ray examination showed distention of the proximal portion of the jejunum. Exploratory laparotomy revealed a distended proximal portion of the jejunum with a thickened, acutely inflamed area in the midportion of the jejunum. A successful resection was done. The pathologic report was as follows: Six inches of jejunum had an acutely and markedly congested serosal surface. The thickened leathery wall showed acute exudative and chronic inflammatory changes. The lumen was constricted to 4 mm.

DIVERTICULA

CASE 5.—A Negro man aged 69 who had an acute condition within the abdomen and high intestinal obstruction refused surgery and died within four days. Necropsy revealed acute diverticulitis with perforation of a diverticulum 4 cm. beyond the duodenojejunal flexure.

CASE 6.—A white woman aged 36 complained of periumbilical pain and vomiting. X-ray examination showed barium sulfate stasis in the lower part of the jejunum with narrowing. Surgery revealed multiple diverticula in the lower jejunal segment; resection was successful.

JEJUNAL ULCERS

CASE 20.—A white man aged 58 complained of an acute condition within the abdomen of five hours' duration. Previous symptoms were suggestive of duodenal ulcer. The right lower quadrant was acutely tender. An exploratory operation revealed a perforated jejunal ulcer 12 inches beyond the ligament of Treitz. Resection and jejunojejunostomy were successful. Pathologic changes included 6 inches of jejunum and a perforated ulcer with chronic proliferative inflammatory changes.

CASE 21.—A Negro girl aged 5 years was markedly anemic with an acute condition of the abdomen and persistent vomiting. Cutaneous ulceration was present. Ascaris lumbricoides was present in the stool. The Wassermann reaction was negative. Autopsy revealed multiple perforated jejunal ulcers (midportion) but no specific microscopic abnormalities.

BENIGN TUMORS

CASE 23.—A white man aged 74 had a sudden onset of high intestinal obstruction. Autopsy revealed a jejunal lipoma causing intussusception.

CASE 24.—A Negress aged 49 had a sudden onset of high intestinal obstruction believed due to previous surgery. Autopsy revealed a fibroma of the jejunum contributing to high intestinal obstruction and acute kinking due to adhesions.

MALIGNANT TUMORS

CASE 30.—A Negro aged 39 complained of periumbilical pain, obstructive symptoms, diarrhea and loss of weight. An exploratory operation revealed an adenocarcinoma of the proximal portion of the jejunum with metastases to the omentum and regional lymph nodes. A palliative gastrojejunostomy was successful.

CASE 31.—A white man aged 56 with umbilical pain of three months' duration, loss of weight, malaise and anemia suddenly

experienced obstructive manifestations. An exploratory operation showed a jejunal neoplasm—not resectable—enterostomy. At autopsy an adenocarcinoma with metastases was found in the proximal portion of the jejunum.

JEJUNAL INTUSSUSCEPTION

CASE 34.—A white girl aged 14½ months suddenly manifested pain, a distended abdomen and bloody diarrhea. Autopsy revealed intussusception of the jejunuum (no anatomic or pathologic cause was demonstrable).

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ABSTRACT OF DISCUSSION

DR. DAVID ADLERSBERG, New York: The paper of Drs. Browne and McHardy proves the increased interest of the gastro-enterologist in lesions of the small bowel and represents a valuable contribution to our knowledge. It is important to realize and emphasize that the jejunum is the site of more extensive enzymatic digestion and absorption than any other part of the digestive tract; thus, pathologic changes of the jejunum are likely to impair the processes of digestion and nutrition to a great extent. It has been also my experience that definite periumbilical pain should call attention to the possibility of a lesion of the small intestine. Intubation with the Miller-Abbott tube and careful fluoroscopic and roentgenographic examination are time-consuming procedures but of essential diagnostic importance. It is agreed that organic lesions of the jejunum such as intussusception, diverticulosis and diverticulitis, primary jejunal ulcer, granuloma of the jejunum (regional jejunitis) and neoplasms (carcinoid, carcinoma, sarcoma and lymphosarcoma) are rare diseases in comparison with other pathologic changes of the gastrointestinal tract. However, it is my belief that milder changes of the jejunum of an inflammatory origin or on the basis of nutritional deficiency are not as infrequent as generally thought. Let me give one example: On gastroscopic examination of patients with gastric resection or gastro-enterostomy, one is frequently struck by the inflammatory changes of the stoma in its gastric as well as in its jejunal portion. In some of these cases the visible jejunitis is more impressive and probably more responsible for the patient's symptoms than the gastritis. One even wonders whether the jejunitis is not a precursor of a marginal ulcer in these cases. In other instances jejunitis cannot be diagnosed by direct visualization, yet an exact history of the case and a careful fluoroscopic and roentgenographic examination of the small bowel will possibly permit an indirect diagnosis.

DR. MAURICE FELDMAN, Baltimore: The roentgen demonstration of jejunal pathologic changes is often confusing because of the technical difficulties encountered in isolating the segments of the jejunum. The same difficulty, however, also holds true in the clinical diagnosis, particularly in the early cases. The information one obtains in the roentgen investigation of the jejunum is almost always the result of late manifestations of the disease. There can be no question that early abnormalities are being overlooked in the vast majority of cases. In this I am in accord with the authors. I should like to emphasize that early roentgen manifestations of disease of the jejunum may be radiologically depicted by a careful painstaking study of the mucosa of the different segments during the transit of the barium sulfate meal. I should like to ask the authors whether they have compiled their data to determine at what stage, particularly in carcinoma, it was possible to demonstrate the condition by means of the roentgen rays.

DR. DONOVAN C. BROWNE, New Orleans: We are all familiar with the work of Dr. Adlersberg on inflammatory lesions of the small bowel and our observations here are in no way contradictory. It is conceivable that such pathologic conditions may occur and especially are they impressive when one sees the changes proctoscopically which may occur in the rectosigmoid following acute infections of the upper respiratory tract. At what stage can the diagnosis of carcinoma be made? It is regrettable that at the time of diagnosis 30 per cent gave evidence of metastases and inoperability, stressing the need for more careful study of the small intestine. Unfortunately, adequate follow-up has not been available.

STILBESTROL-INDUCED GYNECOMASTIA IN THE MALE

CHARLES WILLIAM DUNN, M.D.

PHILADELPHIA

The therapeutic action of stilbestrol in the human being is under investigation by the Council on Pharmacy and Chemistry of the American Medical Association. This case is reported as a contribution toward defining its effect on the human species.

One of the established biologic effects of the naturally occurring estrogens is their growth-stimulating action on certain tissues and organs, one of which is breast tissue. It has also been experimentally established that when estrogenic substance is administered in sufficient amounts it has an inhibitory effect on anterior pituitary lobe trophic functions, among which are the production of growth hormone and the gonadotropic factor. A limited amount of clinical evidence supports these experimental observations.

I [1] have induced gynecomastia in males by administering the natural estrogenic substance. The tissue was studied and reported on by Dr. Charles F. Geschickter.[2] The production of breast development in the female by the administration of natural estrogenic substance has been reported by myself [1] and others. Premature breast development occurred in a girl aged 6 years with gonorrheal vaginitis treated with stilbestrol. Neither hypodermic nor suppository estrogenic therapy could be administered because of the child's physical resistance to these forms of treatment. The child was given 3 drops of stilbestrol solution (1 mg. per cubic centimeter) daily. After six weeks of stilbestrol therapy a mass approximately 2.5 cm. in diameter and 1 cm. in thickness appeared beneath the nipple in both breasts. At this period of therapy the vaginal discharge had disappeared.

I have observed marked breast development in young primary amenorrheal women treated with 5 mg. of stilbestrol daily for from fifty to sixty days. This is evidence that stilbestrol has a growth-promoting action on mammary tissue in the human female.

The present report concerns a male sexual criminal aged 27 years, now incarcerated, with a seven year history of repeated sexual offenses against minor females. Proper permission for the therapeutic experiment was obtained. The initial therapeutic objective in this case was to depress, if possible, the excessive and criminally directed sexual activity of the patient. That the excessive sexual activity was not the result of an increased activity of the so-called central nervous sexual center was indicated by the abnormally high urinary secretion of testis hormone and the gonadotropic factor. The assay report of his urine was 285 bird units of androsterone, 300 rat units of androsterone, 20 rat units of estrogen and 120 rat units of the gonadotropic principle of the urine of pregnant women or of placenta. The abnormally large penis and oversize testes, the sexual history and the hormone assay therefore indicated an anterior pituitary gonadotropic hyperactivity and a resultant increased activity of the testes and production of male hormone.

From the University of Pennsylvania Graduate School of Medicine.

1. Dunn, C. W.: Hormonic Induction of Menstruation in Amenorrheas of from Three Months' to Nine Years' Duration, Am. J. Obst. & Gynec. **30**: 186 (Aug.) 1935.

2. Geschickter, C. F.: Breast Pathology in Relation to Endocrine Disorders in Piersol, G. M., and Bortz, E. L.: Cyclopedia of Medicine, Surgery and Specialties, Philadelphia, F. A. Davis Company, 1939, vol. 9, p. 549.

The patient was given orally 5 mg. of stilbestrol daily, beginning on June 20, 1940 and continuing for a period of sixty days, until a total of 300 mg. had been administered. Because a favorable and desired effect of therapy was obtained, 5 mg. of stilbestrol was then orally administered every other day for a period of thirty-six days. A total of 480 mg. of stilbestrol had been orally administered in a period of ninety-six days without evidence of toxic effect.

At the end of seventy-five days' therapy, when a total of 425 mg. of stilbestrol had been administered, the patient began to have sensitiveness in both nipples and observed a small lump beneath each nipple. During the subsequent twenty-one days the mass beneath the nipple increased progressively in size and sensitiveness and had become painful when he lay on the breasts.

The patient was examined at the end of ninety-six days of therapy, when a total of 480 mg. of stilbestrol had been administered. Physical examination revealed a hard, firm mass beneath the nipple of both breasts, the diameter of which was approximately 6 cm. and its thickness was approximately 2.5 cm. The edge and superior surface of the mass was freely movable beneath the skin, and the mass was separable inferiorly from the pectoral fascia. The mass was regular in outline, well defined and sensitive on palpation. Prior to therapy the breast region had been normal. The physical features of the gynecomastia produced in this male corresponded in character to the breast development produced in the young female child and young adult females to whom stilbestrol was administered.

In my opinion the mammary gland development resulting from the administration of stilbestrol is harder, firmer and of a denser (fibrotic) type of structure. The naturally occurring estrogens produce a breast tissue growth having the physical characteristics of normal breast tissue; these normal breast tissue characteristics are not present in stilbestrol-induced mammary growth. Another important point of differentiation observed is that the stilbestrol-induced breast development resolves at a much more retarded rate than the natural estrogen-induced mammary growth.

A dissimilarity of action of stilbestrol and the follicular hormone in the production of fibroids in the guinea pig uterus has been reported by Lipschutz and Vargas,[3] who state: "This tumorigenic action of stilbestrol is much greater than that of the natural hormones (estradiol and estrone) when equal quantities are compared. . . . The guinea pig uterus increases beyond the normal weight more rapidly with stilbestrol than with the free natural hormones. This is tentatively explained by an inability of the organism to inactivate stilbestrol so rapidly and effectively as estradiol and estriol."

The initial objective of the therapy in this case was to inhibit the hypersexual state. Under the administration of stilbestrol the penis and testes have diminished to approximately two thirds of the pretherapeutic size. The patient states that there is an absence of libido and that masturbation does not produce an ejaculation of seminal fluid.[4] A complete report of the sexual aspect of the case will be reported after urinary bioassays and testicular biopsy have been performed. Stilbestrol therapy is being continued.

3. Lipschutz, A., and Vargas, L.: Tumorigenic Powers of Stilbestrol and Follicular Hormones, Lancet **1**: 543 (March 23) 1940.

4. Testicular biopsy of the right and left testis performed by Dr. Charles W. Charny revealed a generalized degenerative process. There is no evidence of normal cell growth and not a single tubule displays cellular development to the spermatid stage. The intertubular spaces appear to be edematous and contain a reduced number of interstitial cells.

In view of the foregoing subjective and objective clinical observations, it can be reported that stilbestrol produces mammary tissue development to a stage of advanced gynecomastia in the male and also stimulates the growth of mammary tissue in the female. The physical characteristics of the breast tissue reaction of stilbestrol and the naturally occurring estrogenic substances are markedly dissimilar in that the stilbestrol-induced mammary tissue growth is harder, firmer and denser and its rate of resolution after the discontinuance of therapy is markedly retarded as compared with that resulting from the administration of the naturally occurring estrogenic substances.

CONCLUSION

The administration of 480 mg. of stilbestrol to a man aged 27 produced a marked bilateral gynecomastia, the physical characteristics of which were dissimilar to that observed in males treated with the natural estrogenic substances. This dissimilarity of effect was also observed in female patients.

A marked diminution of sexual function, from a hypersexual state to what is considered a hyposexual state, has been obtained.

It is assumed that the therapuetic effect has resulted directly from depression of the anterior pituitary gonadotropic function and indirectly from inhibition of male hormone production in the testes or primary depression of testicular hormone formation. No clinical evidence of other disturbances in anterior pituitary function has been observed.

The administration of 480 mg. of stilbestrol produced no signs of the toxic effects attributed to stilbestrol.

265 South Nineteenth Street.

ALLEGED HEPATOTOXIC ACTION OF STILBESTROL

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E. E. ROSENBAUM, M.D.
AND
SAMUEL SOSKIN, M.D.
CHICAGO

Diethylstilbestrol, the synthetic estrogen which has been named stilbestrol for convenience, has aroused widespread interest because of its remarkable effectiveness in replacement therapy.[1] In addition to possessing most or all of the therapeutic properties of the natural estrogens, it has great potency on oral administration, which makes it a convenient substance to use.[2] However, there has been much concern over the significance of certain side effects which occur in some patients following stilbestrol medication.

Most authors have reported that about 10 to 20 per cent of their stilbestrol-treated patients complained of gastrointestinal distress, principally nausea.[3] The reports

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From the Department of Metabolism and Endocrinology, Michael Reese Hospital.

1. Loesser, A. A.: Therapeutic Trials of Diethylstilbestrol, Brit. M. J. **1**: 13 (Jan. 7) 1939. Winterton, W. R., and MacGregor, T. M.: Clinical Observations with Stilbestrol (Diethylstilbestrol), ibid. **1**: 10 (Jan. 7) 1939. Bishop, P. M. F., Boycott, Muriel, and Zuckerman, S.: The Estrogenic Properties of "Stilbestrol" (Diethylstilbestrol): A Clinical and Experimental Investigation, Lancet **1**: 5 (Jan. 7) 1939. Winterton, W. R.: Clinical Use of Stilbestrol, ibid. **1**: 416 (Feb. 18) 1939.

2. Kellar, R. J., and Sutherland, J. K.: Clinical Experiences with New Synthetic Estrogen—'Stilbestrol' (Diethylstilbestrol): Report to Therapeutic Trials Committee of Medical Research Council, J. Obst. & Gynec. Brit. Emp. **46**: 1 (Feb.) 1939.

3. Buxton, C. L., and Engle, E. T.: Effects of the Therapeutic Use of Diethylstilbestrol, J. A. M. A. **113**: 2318 (Dec. 23) 1939. MacBryde, C. M.; Freedman, Harold, and Loeffel, Ethel: Studies on Stilbestrol, ibid. **113**: 2320 (Dec. 23) 1939. Winterton.[1] Kellar and Sutherland.[2]

correspond with our own experience. Shorr and his associates,[4] on the other hand, have reported a far higher incidence of untoward reactions (approximately 80 per cent), which include skin eruptions, lassitude, headache and psychosis. The last-mentioned authors have also presented some admittedly inconclusive evidence of liver damage in their stilbestrol-treated patients. Using the bilirubin retention and the hippuric acid excretion tests, they found some indication of decreased liver function by the first method but not by the second.

TABLE 1.—*Clinical Results with Stilbestrol Compared to Those Obtained with Estradiol in the Same Group of Menopausal Women*

Case Number	Estradiol, 400 Oral Rat Units Daily	Stilbestrol, 0.5 - 1.0 mg. Daily
1	0	0
2	0	++
3	0	++
4	0	+++
5	++	++
6	++	++
7	++	++
8	+++	+++
9	+++	+++
10	++++	++++
11	++++	++++
12	++++	++++

++++ indicates complete relief.

We report some observations on stilbestrol which, while they do not explain the minor unpleasant reactions which occur in some patients, lead us to believe that the drug is not significantly toxic to the liver.

METHODS AND RESULTS

Our patients were an unselected group of women suffering from the typical menopausal syndrome. In all but a few the menopause was of natural origin. Since the toxicity of a substance has little significance except in relation to its therapeutic dosage, our first work with stilbestrol was an attempt to approximate the latter. Table 1 summarizes our results in a representative group of patients of whom the same ones were treated at different times and after suitable control periods with stilbestrol [5] and estradiol respectively. The number of plus signs indicates our comprehensive judgment of the degree of relief obtained in each instance; 4 plus indicates complete relief of all signs and symptoms. It was our practice to start stilbestrol treatment with 0.5 mg. daily and to raise this dose to 1.0 mg. daily if complete relief was not obtained with the smaller dose. It may be seen that the oral administration of 0.5 to 1.0 mg. of stilbestrol daily yields somewhat better relief of the menopausal syndrome than does the daily ingestion of 400 oral rat units of estradiol.

TABLE 2.—*Bromsulphalein Retention in Stilbestrol-Treated Menopausal Women and in Untreated, Apparently Normal, Women in the Same Age Group*

Stilbestrol-Treated Group					Untreated Control Group		
		Treatment		Bromsulphalein Retention, Percentage			Bromsulphalein Retention, Percentage
Patient	Age, Years	Days	Mg.		Patient	Age, Years	
1. B. L.	36	30	30	10	1. S. S.	57	5
2. R. S.	51	42	46	10	2. I. T.	58	5
3. G. B.	50	168	53	10	3. B. W.	40	10
4. M. H.	47	28	48	15	4. N. L.	41	10
5. H. B.	45	90	82	15	5. L. C.	44	10
6. R. Lo.	49	98	90	15	6. S. P.	52	10
7. L. K.	42	168	112	15	7. S. M.	39	15
8. H. Bi.	45	122	122	15	8. S. Sa.	42	15
9. R. L.	41	196	146	15	9. R. K.	48	15
10. R. C.	55	70	42	30	10. M. M.	41	20
11. S. Sc.	50	196	86	35	11. L. G.	44	20
12. L. D.	54	28	30	60	12. E. M.	57	25

In view of the age group in which our patients fell it seemed inadvisable to select one of the more highly sensitive tests of liver function, which would undoubtedly reveal minor degrees of asymptomatic liver damage in many of our patients whether they were treated with stilbestrol or not. We therefore chose the bromsulphalein retention test, which is generally recognized as being sensitive to liver deficiency of clinically significant degrees. As used by us, 5 mg. of the dye per kilogram of body weight is injected intravenously in one arm. One half hour later a blood sample is withdrawn from the opposite arm. The amount of bromsulphalein remaining in the serum at that time is determined colorimetrically. A retention of 15 per cent is considered to be the upper limit of normal.

Table 2 shows a comparison of the results of the bromsulphalein test in 12 menopausal women who had been treated with stilbestrol for various lengths of time, with the results in an equal number of apparently normal, untreated women in the same age group. Only 3 women in the group treated with stilbestrol and an equal number in the untreated group showed abnormally high bromsulphalein retentions. Nor was there any relationship between the total dose of stilbestrol and the degree of dye retention. It is probable, therefore, that the indicated liver damage was present in the menopausal women before the treatment was instituted.

TABLE 3.—*Bromsulphalein Retention in the Same Menopausal Women, Before and After Treatment with Stilbestrol*

Patient	Age, Years	Treatment: Daily Dose, Mg.	Treatment: Duration, Days	Treatment: Total Dose, Mg.	Bromsulphalein Retention: Before Treatment, Percentage	Bromsulphalein Retention: After Treatment, Percentage
1. S. P.	46	1	21	21	10	10
2. L. C.	48	1	30	30	10	5
3. F. W.	38	1	40	40	10	10
4. S. S.	47	1	42	42	15	10
5. B. B.	47	1	147	147	15	15
6. C. W.	46	5	29	137	35	35
7. E. S.	45	5-10	23	130	40	30
8. A. F.	41	10	8	80	60	30

However, the somewhat greater degree of dye retention in the entire group of menopausal women as compared to the control women suggested the possibility that stilbestrol might have some injurious effect on livers which were already suffering from some slight damage. Bromsulphalein retention tests were therefore done on another group of menopausal women, both before and after they had received stilbestrol. It will be noted in table 3 that in not a single instance was the bromsulphalein retention greater after stilbestrol treatment than before it. In fact, the reverse was true in 4 out of the 8 cases so observed. This seems especially significant in view of the fact that patients 6, 7 and 8 manifested abnormally high degrees of dye retention before treatment and were purposely given 5 to 10 times our usual therapeutic dose of stilbestrol.

At this point in our work it was quite apparent that, as judged by the bromsulphalein retention test, therapeutic doses of stilbestrol did not cause liver damage, nor did they aggravate the preexisting mild deficiencies

4. Shorr, Ephraim; Robinson, F. H., and Papanicolaou, G. N.: A Clinical Study of the Synthetic Estrogen Stilbestrol, J. A. M. A. **113**: 2312 (Dec. 23) 1939.

5. E. R. Squibb & Sons supplied the stilbestrol.

present in some menopausal women. However, none of the women available for this study had manifested any significant clinical signs or symptoms of liver damage. It therefore seemed important to test the possible toxicity of stilbestrol in at least 1 patient (whether menopausal or not) with frank and unquestionable liver disease. The opportunity of a test soon presented itself in J. L., a white man aged 38 who was convalescing from an attack of acute hepatitis.

Before detailing the experimental procedure with the patient just mentioned it is necessary to outline certain animal experiments which, in addition to the observations already presented, had given us sufficient assurance that he would come to no harm.

TABLE 4.—*Indexes of Liver Function in a Dog, Before and After Prolonged Administration of Stilbestrol (10 Mg. Daily for Sixty Days)*

	Before	After
Icterus index	3	3
Serum cholesterol, mg. per 100 cc.		
Total	125	147
Free	41	47
Esters	84 (67.2%)	100 (68%)
Bromsulphalein retention	Less than 5%	Less than 5%
Dextrose tolerance (blood sugar, mg. per 100 cc.)*		
Control	71	50
30 minutes	286	324
60 minutes	145	237
90 minutes	63	121
120 minutes	65	61
150 minutes	74	26
180 minutes	75	51

* 1.75 Gm. of dextrose per kilogram of body weight, injected intravenously in 30 per cent solution.

1. Twelve adult female rats were placed on our usual Purina Fox Chow diet supplemented with 10 per cent powdered milk. In this diet was mixed an amount of stilbestrol which, from the quantities of food eaten each day, resulted in a stilbestrol intake of about 7 mg. per rat daily. At the end of fourteen days the amount of stilbestrol in the diet was doubled, and the new amount was continued for another period of fourteen days. This dose of stilbestrol, when considered in terms of the body weight and life span of the rat, corresponds to a relatively enormous dose over a period of several years in man. Nevertheless the animals were grossly normal when killed for postmortem examinations. The livers and kidneys failed to show any gross or microscopic pathologic conditions, except for the occasional slight, cloudy swelling which may frequently be observed in the tissues of normal rats.

2. To ascertain whether the lack of effect of huge doses of stilbestrol on the cell structure of the liver and kidneys was paralleled by an absence of toxic effect on hepatic function, a similar experiment was done on a dog. This animal ingested 10 mg. of stilbestrol daily for sixty days. Table 4 gives the results of our estimations of the icterus index, serum cholesterol, dextrose tolerance and bromsulphalein retention, both before and after the stilbestrol treatment. There was no evidence of any functional impairment.

Patient J. L. entered the hospital complaining of nausea, vomiting, jaundice, pruritus and clay-colored stools, of three weeks' duration. On physical examination there was slight tenderness in the right upper quadrant of the abdomen. The liver was palpable 4 cm. below the costal margin in the right midclavicular line; the lower edge was smooth and firm. A diagnosis of acute catarrhal jaundice with hepatitis was made. The icterus index at the height of the patient's illness had reached a level of 80, his cholesterol-cholesterol ester ratio was reduced to 27 per cent. He improved, so that three weeks later his icterus index had returned to normal and his cholesterol-cholesterol ester ratio was up to 59 per cent. His bromsulphalein retention at this time was 60 per cent. His symptoms were entirely gone.

The daily administration of 10 mg. of stilbestrol orally was now begun and continued for three weeks. During this period, despite the intake of 210 mg. of the drug, the patient continued to show clinical improvement. By the end of the period the icterus index was still normal, the cholesterol-cholesterol ester ratio had become normal (78 per cent) and the bromsulphalein retention had dropped to 20 per cent.

SUMMARY

With the therapeutic doses (1 mg. daily) and the particular product which we used there was no evidence of any toxic action of stilbestrol on the livers of the menopausal women whom we treated. This was true even with doses of 5 to 10 mg. daily and in women who exhibited some liver dysfunction to begin with as judged by the bromsulphalein retention test. Furthermore, relatively huge doses of stilbestrol in rats and a dog did not give rise to gross or cellular pathologic conditions of liver or kidneys or to liver damage as judged by various criteria of hepatic function. Finally, a patient with indubitable liver damage who was recovering from an attack of acute hepatitis was able to take ten times our usual therapeutic dose of stilbestrol for a period of three weeks without the slightest evidence that his convalescence had been impeded.

It must be concluded that in our experience stilbestrol is not significantly toxic to the liver. We are unable to explain the gastrointestinal distress which follows the use of stilbestrol in some patients. Until this is explained it seems wise to discontinue the administration of stilbestrol in any patient who begins to complain of nausea or other side effects. Meanwhile, there seems to be little reason for withholding the use of a potent and convenient estrogen in such patients as do not experience these side effects.

CLINICAL STUDIES ON STILBESTROL

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In a previous paper [1] we have reported our results on animal experiments concerning the toxicity and activity of stilbestrol. We found that the close similarity of the action of natural and synthetic estrogenic substances on the female sex organs and the pituitary gland of immature, mature and castrated animals could be confirmed. Some evidence of toxicity could be observed in our animals after we administered doses of stilbestrol as low as 0.1 mg. three times a week, although the changes at higher dose levels were not as drastic and alarming as those reported by Loesser.[2] Clinically the drug has been used by numerous investigators of the Continent and recently also in the United States for

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1. von Haam, Emmerich; Hammel, M. A.; Rardin, T. E., and Schoene, R. H.: Experimental Studies on the Activity and Toxicity of Stilbestrol, to be published.

2. Loesser, Arnold: Untersuchungen über die Pharmakologie und Toxikologie synthetischer Brunststoffe (4, 4'-Dioxy-a, b-Diäthylstilben), Ztschr. f. d. ges. exper. Med. **105**: 430, 1939.

the treatment of various ovarian disorders. While the reports on the activity of the drug in the majority of cases are very encouraging, considerable discrepancy exists with regard to the untoward symptoms observed in some patients after its administration. It is the latter fact which up to the present time has caused the American Medical Association to withhold official recognition of stilbestrol. In reporting our own clinical experiences with this drug we shall discuss separately our findings concerning its efficacy together with the pertinent data from the literature and our clinical investigations concerning the toxicity of this drug in human beings.

ESTROGENIC PROPERTIES OF STILBESTROL

First tested on a more extensive scale by Winterton and MacGregor,[3] stilbestrol has proved highly effective in controlling symptoms of menopause. Three patients with kraurosis vulvae were markedly improved. Ten of 11 patients with secondary amenorrhea started to bleed after sufficient therapy. Tüscher [4] treated successfully postpartum amenorrhea with 1.5 mg. once a week. If given to normal women it produced sensitive swelling of the breasts and clitoris with increased libido. Kellar and Sutherland [5] used it for successful control of menopause, senile vaginitis, leukoplakia and secondary abortion. Guldberg [6] was able to produce a normal progestational endometrium by giving a 22 year old castrate woman with intact uterus 20 mg. of stilbestrol for eighteen days followed by 30 rabbit units of synthetic progesterone for six days. Evelbauer [7] reported success of treatment in 50 climacteric patients with comparatively small doses. He did not have any success treating uterine hypoplasia and amenorrhea and recommended the natural estrogen for patients with these conditions. Buschbeck and Hausknecht [8] reported success in cases of amenorrhea with total doses of as little as 20 mg., given in 5 mg. doses. A similar experience was reported by Heisler.[9] Engelhart [10] induced "menstruation" in castrate women. Brühl [11] treated successfully endometrial hemorrhages with 2 to 3 mg. of stilbestrol. He also had success in the treatment of dysmenorrhea, dyspareunia and lack of libido. According to Lindemann [12] the estrus produced by diethylstilbestrol dipropionate lasted twice as long as the one produced by estradiol benzoate. Varangot [13] found stilbestrol three times as effective as crystalline estrone if given by injection and six times as active as estradiol benzoate when given by mouth. In 18 cases improvement was achieved by daily doses of 0.3 mg. The danger of overdosage was stressed by Ehrhardt, Kramann and Schäfer.[14] They found 12 mg. of stilbestrol

TABLE 1.—*Clinical Summary of Stilbestrol in the Treatment of the Menopause*

	Series A	Series B
1. Total number of patients treated	58	67
Age		
Below 30	3	2
Between 30 and 40	19	9
Between 40 and 50	29	37
Over 50	7	19
Diagnosis		
Surgical menopause	31	24
Natural menopause	26	43
Climacteric condition	1	11
2. Form and duration of therapy		
Total doses		
1 to 20 mg.	24	48
20 to 50 mg.	26	15
50 to 100 mg.	8	3
Over 100 mg.	0	1
Single doses		
Oral (less than 1 mg.)	30	33
Oral (more than 1 mg.)	2	5
Parenteral (less than 1 mg.)	5	4
Parenteral (more than 1 mg.)	18	37
Duration		
Up to 1 month	17	35
1 to 3 months	23	25
3 to 6 months	16	7
6 months to 1 year	2	0
3. Results		
Good: complete relief of all symptoms	18	48
Fair: partial relief of all symptoms	21	8
Poor: no or little relief	17	
Adverse: addition of toxic symptoms made patient feel worse than before	2	9
4. Comparison with other therapy		
Number of patients treated previously with other estrogenic substances	22	50
Patients reporting better response	7	25
Patients reporting equal response	4	17
Patients reporting worse response	11	12
5. Toxic symptoms after stilbestrol therapy		
Total number of patients complaining	28	24
Nausea and vomiting	22	22
Colitis—diarrhea	0	2
Headaches or dizziness	12	3
Drowsiness or weakness	4	10
Nervousness—excitement	2	3

TABLE 2.—*The Effect of Stilbestrol on the Urinary Bioassay*

	Number of Cases	Gonadotropic Excretion in 24 Hours: Over 50 Mouse Units	Gonadotropic Excretion in 24 Hours: Trace	Gonadotropic Excretion in 24 Hours: Negative	Theelol Excretion in 24 Hours: Over 100 Mouse Units	Theelol Excretion in 24 Hours: Trace	Theelol Excretion in 24 Hours: Negative
Before treatment	35	51%	26%	23%	3%	11%	86%
After treatment of at least 1 month	11	27%	9%	64%	55%	18%	27%

TABLE 3.—*Survey of Toxic Symptoms Observed in the Literature*

Author	Total Number of Cases	Number of Toxic Reactions	Percentage	Comment
Winterton and MacGregor	24	6	25	Nausea
Loesser	11	2	18	Nausea
Kellar and Sutherland	15 (?)	3	20	Transient nausea
Varangot	18	13	87	Late and early symptoms; 4 cases of absolute intolerance
Bishop et al.	46	3	65	Nausea and headaches
Shorr et al.	44	35	80	In 14 therapy had to be stopped
Kurzrok et al.	40	26	65	In 10 therapy had to be stopped; nausea, malaise
MacBryde et al.	37	8	22	Nausea and 3 cases of vomiting
Karnaky	180	Occasionally	..	Nausea
Geist and Salmon	38	8	21	Anorexia, dizziness, vomiting
Burton and Engle	17	1	6	

3. Winterton, W. R., and MacGregor, T. N.: Clinical Observations with Stilbestrol (Diethylstilbestrol), Brit. M. J. **1:** 10, 1939.

4. Tüscher, H.: Behandlungserfolge mit Cyren bei Ovarialinsuffizienz nach der Schwangerschaft, Klin. Wchnschr. **18:** 808, 1939.

5. Kellar, R. J., and Sutherland, J. K.: Clinical Experiences with a New Synthetic Estrogen—"Stilbestrol" (Diethyl-Stilbestrol), J. Obst. & Gynaec. Brit. Emp. **46:** 1, 1939.

6. Guldberg, Erik: Echte Menstruation bei einer kastrierten Frau nach Zufuhr von synthetische hergestellten Hormonstoffen, Zentralbl. f. Gynäk. **62:** 2584, 1938.

7. Evelbauer, K.: Zur Behandlung mit Stilbenpräparaten. München. med. Wchnschr. **86:** 1118, 1939.

8. Buschbeck, H., and Hausknecht, K.: Ueber die Wirkung von Stilboestrol beim Menschen, Klin. Wchnschr. **18:** 160, 1939.

9. Heisler, Wolfgang: Die Behandlung der Amenorrhöe mit körperfremden Wirkstoffen, Med. Klin. **35:** 713, 1939.

10. Engelhart, E.: Der Aufbau der Proliferationsschleimhaut bei der kastrierten Frau durch einen synthetischen oestrogenen Wirkstoff, Wien. klin. Wchnschr. **51:** 1356, 1938.

11. Brühl, K.: Erfahrungen mit der therapeutischen Anwendung der Cyrene, synthetischer Präparate mit den Wirkungen des weiblichen Sexualhormons, München. med. Wchnschr. **86:** 582, 1939.

12. Lindemann, W.: Ueber Cyren—"Bayer"—und seine Wirkung auf die Milchstauung und zur Laktationsbeeinflussung, Zentralbl. f. Gynäk. **63:** 719, 1939.

13. Varangot, M. J.: Activité oestrogène et toxicité du 4:4' dihydroxy a:b diéthyl-stilbène (stilboestrol), Bull. Soc. gynéc. et d'obst. **28:** 160, 1939.

14. Ehrhardt, K.; Kramann, H., and Schäfer, H.: Vorläufige klinische Ergebnisse mit östrogenen Stilben-Präparatan, München. med. Wchnschr. **86:** 261, 1939.

sufficient to produce a normal proliferating endometrium and recommended 0.5 to 1 mg. as single doses and 2 to 5 mg. as a weekly dose for the treatment of the menopause. Bishop, Boycott and Zuckerman [15] produced withdrawal bleeding in 8 patients with amenorrhea and rhythmic hemorrhages in 2. Biopsy of the breast after administration of 280 mg. by mouth showed epithelial proliferation with no increased secretory activity. In their summary Bishop and his co-workers emphasized the close resemblance of the effect of stilbestrol to that of natural estrogen. Both produce withdrawal bleeding, a proliferative type of endometrium, growth of the hypoplastic uterus, relief of the menopausal syndrome, conversion of the vaginal smear into the estrous type, restoration of the vulva and vagina to normal, proliferation and activation of the mammary glands with painful swelling of the breasts and relief of dysmenorrheic pains. Cessation of lactation after administration of stilbestrol in cases of stillbirth was reported by Tietze [16] and Lindemann.[12] Peel [17] showed that stilbestrol had little value in inducing labor although it was definitely advantageous in increasing the tone and uterine contractions.

In the United States six reports have appeared up to the time this report was written on clinical trials with stilbestrol. Shorr, Robinson and Papanicolaou [18] studied its effect on forty-four women, many of whom had been treated previously with natural estrogens, and confirmed its powerful estrogenic action. Only 2 of the 44 patients failed to show an estrous type of vaginal smear. They found that 1 mg. of stilbestrol was equivalent to 1.7 mg. of estrone and emphasized the great advantages of oral administration. Kurzrok and his co-workers [19] studied 40 cases of various gynecologic disorders. Fifteen menopausal patients obtained symptomatic relief, sometimes as early as twelve hours after the initial treatment. In the other 25 cases of amenorrhea, oligomenorrhea, dysmenorrhea and uterine hypoplasia the therapeutic effect of stilbestrol was identical with the one produced by the natural estrogen. MacBryde, Freedman, Loeffel and Allen [20] studied 37 cases of various types of ovarian deficiency. They were able to produce withdrawal bleeding and mammary growth at will. Implantation of pellets weighing 100 mg. each to 6 castrated patients produced an estrous type of vaginal smear within two days and endometrial proliferation within seven days. The menopausal symptoms were greatly relieved as long as the pellets remained in place. The average daily absorption could be determined as ranging from 0.127 to 0.250 mg. Karnaky [21] treated 189 patients with menstrual disorders. He found stilbestrol as effective as natural estrogens. Geist and Salmon [22] used the drug in 38 menopausal women in doses of 1 to 5 mg. three times a week or in tablets of 3 to 5 mg. daily. The women showed a positive vaginal smear as early as four days after treatment and a complete control of hot flashes. However, headaches and nervousness were not strikingly relieved.

TABLE 4.—*Effect of Stilbestrol on Blood of Six Patients*

	Week	S. B.	T. S.	V. W.	L. H.	M. A.	C. T.
Doses	...	16 mg.	24 mg.	24 mg.	24 mg.	24 mg.	24 mg.
Results	...	Severe nausea	Severe nausea	Sick twice; felt improved	Sick twice; good results	Some nausea; good results	No nausea; good results
Red blood cells in millions per cubic millimeter	1	3.59	4.78	5.30	5.12	5.72	4.05
	2	3.49	5.10	4.96	4.38	4.82	4.35
	3	4.21	5.45	4.22	3.70	4.97	4.67
	4	3.68	4.37	4.57	4.66	4.45	3.56
Hemoglobin in grams per hundred cubic centimeters	1	10.9	13.1	13.7	16.7	15.8	13.1
	2	10.9	15.6	13.2	14.4	16.2	12.0
	3	12.0	15.3	12.8	13.7	16.0	10.9
	4	12.0	13.7	15.3	15.7	15.6	13.4
Percentage of reticulocytes	1	0.6	0.4	1.4	2.4	3.6	0.4
	2	0.4	0.4	0.8	3.6	1.8	1.8
	3	0.6	2.4	1.0	1.6	0.8	2.4
	4	1.0	2.0	2.4	4.6	0.2	2.0
Leukocytes in thousands per cubic millimeter	1	6.40	10.20	7.30	9.70	6.45	6.50
	2	5.85	9.45	7.80	9.65	8.60	8.80
	3	4.85	12.00	7.40	9.10	7.85	10.15
	4	5.30	10.40	6.80	10.20	7.35	9.00
Thrombocytes in hundred thousands per cubic millimeter	1	3.73	7.98	6.99	5.75	6.52	5.67
	2	4.74	5.10	3.96	6.48	7.13	6.27
	3	4.96	8.28	3.03	5.22	5.23	2.53
	4	5.66	7.38	5.11	2.98	4.00	8.44

In our clinical studies a series of 125 patients with surgical and natural menopause were treated from two weeks to six months with doses ranging up to 60 mg. (table 1). Series A is composed of patients studied at the endocrine clinic of the University Hospital; series B comprises patients treated in private practice. We thought a separation of our material into these two groups might be of interest since a marked difference existed between these patients with respect to the presentation of their symptoms and of any subsequent changes. The stilbestrol was administered in the majority of cases by oral therapy in daily doses of 0.2 to 0.5 mg. This was found to be the most effective type of treatment as it produced the least amount of disagreeable symptoms. Parenteral therapy was usually used in doses of 1 mg. twice a week. The duration of treatment extended in the majority of cases from one to three months. Only 2 patients had therapy for one year.

Our results showed a considerable difference between the patients of series A and B, justifying the division

15. Bishop, P. M. F.; Boycott, Muriel, and Zuckerman, S.: The Estrogenic Properties of "Stilbestrol" (Diethylstilbestrol), Lancet **1**: 5, 1939.

16. Tietze, K.: Zur Einführung des Cyrens in die Therapie hormonaler Störungen der weiblichen Genitalfunktion, Geburtsh. u. Frauenh. **1**: 486, 1939.

17. Peel, J. H.: The Effects of Stilbestrol on Labor, Proc. Roy. Soc. Med. **32**: 1230, 1939.

18. Shorr, Ephraim; Robinson, F. H., and Papanicolaou, G. N.: A Clinical Study of the Synthetic Estrogen Stilbestrol, J. A. M. A. **113**: 2312 (Dec. 23) 1939.

19. Kurzrok, Raphael; Wilson, Leo, and Perloff, W. H.: The Action of Diethylstilbestrol in Gynecological Dysfunctions, Endocrinology **26**: 581, 1940.

20. MacBryde, C. M.; Freedman, H.; Loeffel, E., and Allen, D.: Estrogenic Therapy by Implantation of Stilbestrol Pellets, Proc. Soc. Exper. Biol. & Med. **43**: 212, 1940.

21. Karnaky, K. J.: Stilbestrol, the New Synthetic Estrogenic Hormone, Urol. & Cutan. Rev. **43**: 633, 1939.

22. Geist, S. H., and Salmon, U. J.: Indications for Estrogen Therapy, New York State J. Med. **39**: 1759, 1939.

of our material. While 71 per cent of the patients of series B reported complete relief of all symptoms, only 30 per cent of our charity patients were content with the therapy. Poor or adverse results were obtained in only 13 per cent of the privately treated patients, while it was present in 32 per cent of the patients treated at the clinic. The reason for this marked discrepancy is probably a less careful selection of suitable material in series A, since the mental capacity of our patients often makes proper recognition of the menopausal syndrome difficult. Economic factors and social problems may also have some part in the differences in our therapeutic results. Eighty-one patients of both series had had previous experience with other estrogenic drugs. Thirty-two per cent of series A and 42 per cent of series B reported better results after stilbestrol than

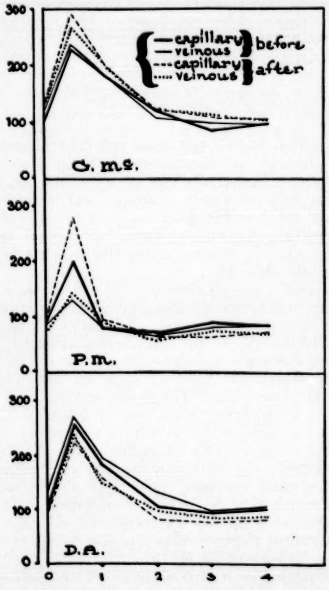


Chart 1.—Dextrose tolerance curves before and after administration of stilbestrol in 3 patients.

with any other estrogenic substance tried. A total of 25 per cent reported an equal result, while 28 per cent reported less success.

As objective signs of improvement we have taken the decrease or disappearance of the gonadotropic substance in the urine of pregnancy and the appearance of estrus as evidenced by the vaginal smear method and the determination of the urinary estrogens. From table 2 we learn that 64 per cent of the patients treated at least for one month with stilbestrol showed no significant amount of gonadotropic substance in the urine as contrasted to only 23 per cent of the untreated control group, while over half of the treated patients showed a large amount of estrogenic substances. The vaginal smear changed in almost all instances within the first week of treatment from a menopausal to an estrogenic type. Changes in the endometrium were not observed as early or as consistently, and we wish to withhold further comment on this until more studies have been accomplished. Excessive stimulation of the sexual organs was found in a sufficient number to be worth mentioning. The most alarming symptom was the appearance of vaginal bleeding, which was noticed in 8 cases. It occurred in patients who at the time of treatment were one and a half years past the last men-

TABLE 5.—*Laboratory Tests in Patients Treated with Stilbestrol*

Laboratory Test	Normal Control	After Therapy
Icterus index	3-9	2-9
Prothrombin determination	80-90	85-100
Weltmann coagulation band	1-7	3-6
Serum bilirubin	0.2-1.5	0.2-0.2
Blood chlorides	462.9-519.8	346-519.8
Bromsulphalein	2%-20%	4%-7%
Creatinine	1.2-1.5	1.2-1.6
Blood urea nitrogen	14-30.3	10-28.5
Sedimentation rate	0.4-1	0.4-1.7

strual period and lasted up to twenty-one days. Curettement revealed a moderate or marked proliferation of the endometrium without evidence of the secretory phase. Vaginal discharge was observed in 7 cases. Mammary symptoms consisting of painful fulness of the breast, and some nodular swellings were present in 5 cases. Increased sexual stimulation was present in 3 cases. In those climacteric women who were still menstruating while under treatment, stilbestrol therapy affected the menstruation. Three menstrual periods were delayed, and one stopped; in 11 cases cramps accompanying the period were increased or appeared, and at the same time the patient complained of headache.

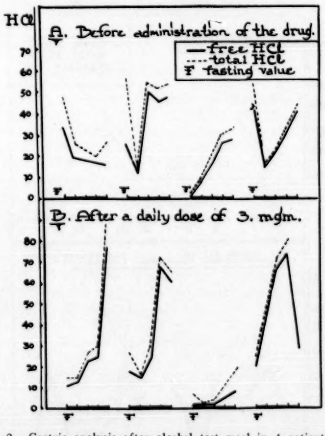


Chart 2.—Gastric analysis after alcohol test meal in 4 patients treated with small doses of stilbestrol.

We may say that stilbestrol has proved to us, in the doses administered orally to patients, a powerful estrogenic substance. It is our opinion that most of the doses recommended so far in the literature are excessive and that smaller doses should be used. We believe also that its continuous administration is unnecessary and that it should best be spaced at regular intervals. By using discretion in its administration an excessive stimulation of the sexual organs can well be avoided,

although this stimulation seemed in no way harmful and in no way different from the effects produced by excessive doses of natural estrogen. We feel, furthermore, that the more intelligent type of patient, who shows better cooperation with the physician, will receive greater advantages from the treatment.

CLINICAL STUDIES OF TOXICITY

Already the earliest investigators of stilbestrol have observed that its oral administration caused a number of untoward symptoms in patients which were sometimes so pronounced that the administration of the drug had to be discontinued. Reports of the incidence of these so-called toxic effects vary and are probably dependent a great deal on the type of patients and the carefulness of clinical observation. In the brief tabulation of the toxic symptoms as cited so far in the literature we observe a remarkable variation of incidence reported by the various authors (table 3). The symptomatology of stilbestrol has been best studied by Shorr, Robinson and Papanicolaou [18] and by Varangot.[13] Shorr and his associates found lassitude the most prominent symptom. They observed in their series 6 patients with vertigo, 8 with erythema, 1 with toxic psychosis, 1 with paresthesia and 1 patient afflicted with unquenchable thirst. As a rule these symptoms persisted, and a second course of treatment was tolerated as poorly as the first. Toxic reactions were also obtained two to three hours after injection of stilbestrol. Their appearance could not be correlated with any critical level, and Shorr and his associates postulated that all indications pointed to an injury to the central nervous system as their cause. Varangot distinguished between early and late toxic symptoms after administration of stilbestrol.

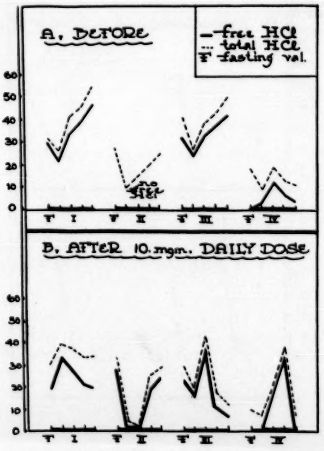


Chart 3.—Gastric analysis after alcohol test meal in 4 patients treated with nauseating doses of stilbestrol.

Usually the patient was taken ill on the second day with feelings of nausea and vomiting. Even if the administration of stilbestrol was immediately stopped, the complaints persisted for one to two days. Continuation of treatment made the complaints more accentuated. The late symptoms, which set in after two months of treatment, consisted of burning gastric pain occurring after meals with nausea, vomiting and vertigo. Loss of appetite and general malaise were present, and the patient urgently insisted on discontinuance of the therapy.

Available laboratory reports have so far failed to show any tangible evidence of toxicity in human beings. The

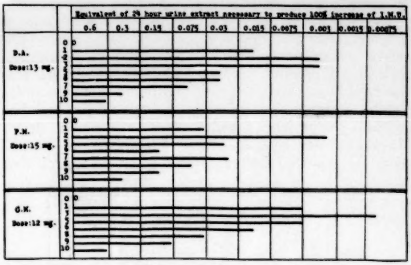


Chart 4.—Urinary excretion of stilbestrol, in 3 patients after injection of 1 mg. to 10 pounds (4.5 Kg.) of body weight. I. M. U., infantile mouse uterus.

tests involved include red blood cell counts; leukocyte counts; hemoglobin determinations; urinalyses; serum protein determinations; icterus index and van den Bergh reactions; bromsulphalein, galactose and hippuric acid tests, and prothrombin determinations (MacBryde and his co-workers, Buxton and Engle [23] and Shorr and his co-workers). No evidence of allergic or urticarial phenomena was obtained.

In section 5 of our clinical summary (table 1) the so-called toxic symptoms encountered during treatment with stilbestrol are analyzed. A total of 52 patients, or approximately 42 per cent, complained of some untoward symptoms during treatment. In the majority of cases nausea and vomiting were the principal and only cause of complaint. Headaches and dizziness rated second in importance. One case of psychotic excitement and 2 cases of severe diarrhea occurred during stilbestrol therapy. One exceedingly sensitive patient had a severe local reaction consisting of vaginal discharge, cystitis, backache, itching of the vulva and marked stimulation of the breast on a total dose of 3 mg. given orally in 0.5 mg. doses for six days. In another patient there developed in the course of treatment a galactocele of the breast.

In the clinical evaluation of the aforementioned symptoms we may state that although they were decidedly disagreeable they appeared not in any way seriously harmful and disappeared in all instances as soon as treatment with stilbestrol was discontinued. They could be observed either immediately after the first administration of the drug or shortly thereafter and were likely to develop more frequently after oral administration, although parenteral administration occasionally produced them. Reduction in the dose usually decreased the severity of these symptoms sufficiently so that the patient could carry on with the treatment. Only in 9 cases were we forced to discontinue the therapy. Our attempt to avoid the gastrointestinal symptoms by administering the drug in enteric coated tablets has met with failure so far; 5 out of the 6 patients treated in this manner became nauseated.

A series of clinical investigations was undertaken with the purpose of discovering definite evidence of toxicity

23. Buxton, C. L., and Engle, E. T.: Effects of the Therapeutic Use of Diethylstilbestrol, J. A. M. A. **113**: 2318 (Dec. 23) 1939.

of the drug in the doses administered to human beings. Our study was conducted on men and women patients who were admitted to the hospital and treated with doses of stilbestrol. Repeated, and in one instance daily, blood counts were done with determinations of all formed elements in the blood. Although occasionally an abnormally low value was obtained, such as 152,000 for thrombocytes or 3,500,000 for red blood cells, in no instance could any evidence of a permanent injury to the blood be obtained (table 4). A specimen of bone marrow which we took for biopsy from a patient with a low red blood cell count showed hyperplasia of the erythropoietic elements and a small increase in the monocytes and eosinophil myelocytes. The blood sugar curves determined on 3 patients who obtained one single large dose of stilbestrol showed no consistent changes in the dextrose tolerance (fig. 1).

Because of the predominance of gastrointestinal symptoms gastric analysis was performed before and after administration of stilbestrol. In one group of patients small doses which did not produce any nausea were given over three days. Although the acid value while the patient was fasting was lower than before administration of the drug, the acidity rose to a higher peak after an alcohol test meal (fig. 2). We then administered to 4 patients doses of 10 mg. daily, which produced severe nausea with vomiting. The analysis of the gastric secretion showed irregular curves, which, however, inclined more to the side of hypoacidity (fig. 3). With reference to our animal experiments in which we definitely observed mucosal atrophy of the stomach after toxic doses, we suggest that small doses of stilbestrol may exert an irritating effect, while large doses have a depressing effect on the gastric secretion. It is the latter factor which probably is responsible for the nausea.

All other laboratory tests which were done on the patients before and after treatment with stilbestrol failed to show any evidence of organic injury (table 5). The liver function, as determined by the icterus index, the prothrombin level of the blood, the Weltmann coagulation band, the serum bilirubin and the bromsulphalein test, was normal in all our patients. The kidney function, as determined by the blood urea nitrogen and the blood creatinine, was not impaired. The urine of the patients showed in no instance albumin or casts. The blood chlorides (Selye [24]) were not changed.

In order to determine the fate of the injected stilbestrol, the excretion of the substance was determined quantitatively in the urine and feces of 3 patients who received one large dose of the drug (10 to 15 mg.). Figure 4 shows the daily excretion in the urine as measured by the equivalents of twenty-four hour urine extracts which were necessary to produce 100 per cent increase of the infantile mouse uterus.[25] The excretion of the drug in the urine begins immediately after its administration, reaches its highest levels on the third to the fifth day and decreases rapidly to a small amount, which then can be found in the urine for some time. We carried on the determinations for sixteen to twenty days, until even the last trace of the substance had disappeared. The feces during this period gave a strong estrogenic reaction, and we must assume that a considerable portion of the ingested stilbestrol is excreted with the feces. An approximate calculation of the excreted amount would suggest that from 10 to 30 per cent of the ingested stilbestrol was excreted within the first ten days after its administration.

24. Selye, Hans: On the Toxicity of Oestrogens with Special Reference to Diethylstilbestrol, Canad. M. A. J. **42**: 48, 1939.
25. von Haam, Emmerich: The Direct and Indirect Determinations of Estrogenic and Gonadotropic Hormones, Am. J. Clin. Path. **10**: 205, 1940.

SUMMARY AND CONCLUSIONS

One hundred and twenty-five patients with surgical and natural menopause were treated from two weeks to six months with doses ranging up to 60 mg. of stilbestrol. In 75 per cent of the cases excellent or good results were obtained, with 39 per cent of the patients reporting better response to this therapy than to any other estrogenic substance used previously. In 42 per cent of the patients some untoward symptoms appeared during the therapy. These, however, could be controlled in the majority of cases by reducing the dose, and the treatment had to be discontinued in only 9 cases.

Laboratory investigation of the function of the parenchymatous organs and of the erythropoietic system did not reveal any evidence of organic injury. A gastric analysis showed a slightly decreased response of the mucosa to the alcohol test meal after the administration of nauseating doses of the drug. Ten to 30 per cent of the ingested stilbestrol was excreted in the urine and feces during the first ten days following its administration.

We feel that because of the ease of administration and the great economic advantages stilbestrol has a definite place in the treatment of the menopause provided that small doses are used and that the therapy is not continued over too long a time.

Clinical Notes, Suggestions and New Instruments

DERMATITIS DUE TO A FACE POWDER CONVEYOR

LESTER HOLLANDER, M.D., PITTSBURGH

Mrs. R. H., aged 49, an American housewife, referred to me by Dr. Charles E. Hays of Johnstown, Pa., on May 7, 1940, presented a sharply defined, vesiculo-erythematous eruption which involved the nose, the upper lip and the adjacent portion of the right lower eyelid. The tip of the nose and the central furrow of the upper lip were thickened and cracked, these being the areas of the most marked involvement. The eruption was of approximately four months' duration and it was exceedingly itchy.

It was evidently due to some sensitizing contact substance, but neither the history of the onset and course nor any variability in the intensity of the subjective symptoms gave me any clue except that the substance had something to do with the face and especially with the nose.

Accordingly the patient was instructed to stop the use of her cosmetics, soap, handkerchiefs and cleansing tissues for a period of two weeks. At the expiration of that period she returned; her face was practically clear, indicating that I was on the right track. Patch tests were now done with all the interdicted substances and articles, including face powder, rouge, lipstick, nail lacquer, cleansing and tissue creams, perfume, wave set, soap and cleansing tissue. These were negative at the end of forty-eight hours and also at the end of one week.

Because of the clinical improvement after the discontinuance of her cosmetics and soap she was instructed to return to the use of these singly, one week apart, so as to ascertain the cause as the eruption would reappear.

On August 7 she returned with a marked recurrence of the eruption. I was unable to trace back the irritant because, after being free from the eruption for a few weeks, the patient returned to her regular cosmetic and cleansing routine.

I decided to retest her to her cosmetics. In obtaining the various samples for the patch tests her face powder was pro-

From the Pittsburgh Skin and Cancer Foundation.

duced from a rubber sponge powder puff. It was rounded and biscuit-like with a central pocket reached through a lateral slit. The porous quality of the rubber permitted the escape of the face powder when the skin was patted with the puff. She bought this puff shortly before the original onset of this eruption and used the puff to powder her nose only when she was away from her home. The outline of the eruption was confined to the area of its use.

Patch tests of the puff, with and without the face powder, were strongly positive in twenty-four hours, while the patch test of the face powder alone was again negative.

This case is of interest because a dermatitis was produced by a conveyor of a cosmetic, a rubber sponge powder puff, and there is no mention of such an occurrence in the literature.

631 Jenkins Building.

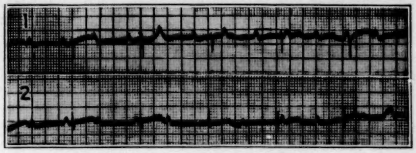
PRENATAL DIAGNOSIS OF COMPLETE CONGENITAL HEART BLOCK

CLYDE J. GEIGER, M.D., AND LAURENCE E. HINES, M.D.
CHICAGO

About seventy cases of congenital heart block have been recorded. Yater's [1] review of cases prior to 1929 included only thirty cases of well established block. The criteria used by him and in subsequent reviews were auriculoventricular dissociation proved by a graphic method in a relatively young person, development of bradycardia at a fairly early age, and absence of a history of infection which might cause heart block. In 1934 Hays [2] collected twelve additional cases. Since then about twenty-six additional cases have been reported. The age at which the diagnosis of heart block has been made varies from birth up to 20 years. Only five cases including our case have been diagnosed before birth. Yater,[1] Witt,[3] Heubner [4] and Ottow [5] have made a prenatal diagnosis of complete heart block. The diagnosis of heart block before birth has also been made by White, Eustis and Kerr,[6] Maclellan,[7] Dippel,[8] Kriszt [9] and Philipp,[10] but these were reports of partial (not complete) heart block.

REPORT OF CASE

Mrs. F. H., a white primipara aged 30, a patient of Dr. E. W. Mosley, was admitted to the obstetric service at St. Joseph Hospital Dec. 2, 1939. Her antepartum course had been uneventful. She had had no serious illnesses or operations in the past. She was well nourished and presented the usual manifestations of pregnancy at full term, blood pressure 116 systolic, 86 diastolic, a negative Wassermann reaction, a normal blood count and normal urine. At the time of admission the bag of waters was intact, the head was not engaged, labor pains were mild and irregular and the fetal heart tones were 136 per minute. Two hours after admission the labor pains were still mild and irregular. No engagement of the head had taken place but the fetal heart tones had dropped to 64 per minute. The slow fetal heart rate varying from 58 to 64 per minute persisted until the time of delivery, which occurred nineteen hours after admission. At first the sharp drop in fetal heart rate caused suspicion of impending fetal asphyxia. However, the persistence of regular forceful beats between pains was not characteristic of asphyxia and a diagnosis of heart block was considered and labor was allowed to proceed normally. A healthy female infant weighing 3,180 Gm. delivered spontaneously forty-eight minutes after the beginning of the second stage of labor. The baby and mother were discharged in apparent good health nine days after the birth. The infant was well nourished and healthy. There was no cyanosis, no enlargement of the heart, no murmurs and no abnormal accentuations. Repeated electrocardiograms, one of which is shown in the illustration, revealed complete heart block with an auricular rate of 120 and a ventricular rate of 60, right axis deviation and flat T waves in all leads. A roentgenogram of the chest revealed a heart and aorta of normal size and contour. The retrocardiac space was clear. The lung fields were well aerated. April 1, 1940, the baby was in good health except for the heart block, which a recent electrocardiogram showed was still present.



Leads 1 and 2 of electrocardiogram.

Review of Previously Reported Cases of Prenatal Diagnosis of Heart Block

Author	Sex	Slowest Fetal Heart Rate	Slowest Rate After Birth	Time of Prenatal Diagnosis	Malformations	Heart Enlargement	Proof of Block	Cyanosis	Duration of Life	Other Observations
Yater 1929	♂	47	47	2 weeks	Numerous anomalies (autopsy)	0	Positive electrocardiogram	4 plus	18 days	Died in cyanotic attack
Witt 1934	♂	44	44	2 months	Coarctation of aorta; endocardial defect (autopsy)	4 plus	Positive electrocardiogram	4 plus	75 days	Died in cyanotic attack
Heubner 1938	No record	80	60	Not given	None	0	Positive electrocardiogram	0	Living at 11 months (healthy)	Block disappeared at 11 months
Ottow 1939	♀	32	52	24 hours	None	1 plus (left)	Positive electrocardiogram	0	Living at 5 months (healthy)	Block still present at 5 months
Geiger and Hines 1940	♀	58	60	17 hours	None	0	Positive electrocardiogram	0	Living at 5 months (healthy)	Block still present at 5 months

COMMENT

Prenatal diagnosis of complete heart block has been reported only five times. The accompanying table includes the important information in the five reported cases. The time of diagnosis prior to birth varied from seventeen hours to two months. In all instances the diagnosis was made by detection of an unusually slow regular fetal heart rate (32 to 80). All

1. Yater, W. M.: Congenital Heart Block: Review of Literature; Report of Case with Incomplete Heterotaxy; Electrocardiogram in Dextrocardia, Am. J. Dis. Child. **38**: 112-136 (July) 1929.
2. Hays, Luvern: Report of Three Cases of Congenital Heart Block with Résumé of Literature to Date, J. Pediat. **4**: 380-386 (March) 1934.
3. Witt, D. B.: Congenital Complete Auriculoventricular Heart Block, Am. J. Dis. Child. **47**: 380-387 (Feb.) 1934.
4. Heubner, Dietrich: Ueber die Bedeutung von Herzblock bei Neugeborenen, Ztschr. f. Kreislaufforsch. **30**: 600-602 (Aug. 15) 1938.
5. Ottow, Benno: Intrauterine Wahrscheinlichkeitsdiagnose eines Herzblocks bei der Frucht—klinisch am Neugeborenen bestätigt, Zentralbl. f. Gynäk. **63**: 715-719 (April 1) 1939.
6. White, P. D.; Eustis, R. S., and Kerr, W. J.: Congenital Heart Block, Am. J. Dis. Child. **22**: 299-306 (Sept.) 1921.
7. Maclellan, E. K.: Double Placenta Praevia (Binovular Twins) and Prenatal Diagnosis of Congenital Heart in Successive Labors, Brit. M. J. **1**: 14-15 (Jan. 5) 1935.
8. Dippel, A. L.: Two Cases of Congenital Heart Disease in Which Diagnosis Was Made Before Birth, Am. J. Obst. & Gynec. **27**: 120-123 (Jan.) 1934.
9. Kriszt, Josef: Angeborener sino-aurikulärer Block bei einem Neugeborenen, Zentralbl. f. Gynäk. **61**: 2515-2518 (Oct. 23) 1937.
10. Philipp, Ernst: Angeborener kindlicher Herzfehler, intrauterin wahrgenommen, Ztschr. f. Geburtsh. u. Gynäk. **91**: 665-668, 1927.

diagnoses were confirmed by electrocardiograms, which showed complete auriculoventricular dissociation. In our case a differentiation between asphyxia and heart block was necessary because the onset of block occurred during the course of labor. Asphyxia as the cause of fetal bradycardia was ruled out in this case because the rate was constant and the strength and regularity were not influenced by uterine contractions.

Necropsies on patients with congenital heart block usually have shown congenital malformations. Two patients of this series died and autopsies revealed congenital anomalies in each. Both fatal cases also showed typical clinical evidence of congenital defects, as evidenced by cyanosis, murmurs and enlargement. However, the other three, all living, showed no clinical evidence of congenital defects, and it is possible that other transient lesions of the bundle of His may cause the block. Hemorrhage or toxic or inflammatory lesions might reasonably produce a temporary defect. This is suggested by the termination of the block in Heubner's case and also by the termination of partial block in other cases. The absence of toxemia in the mother and the development of the block early in labor lend no support to hemorrhage or infection as an etiologic factor in our case.

The presence of cyanosis and of other signs of congenital heart defects in patients with complete congenital heart block points to an early unfavorable prognosis. If the block is not associated with clinical evidence of congenital defects, the health of the child may be unimpaired and the prognosis less serious.

SUMMARY

A case of complete heart block was diagnosed before birth. A sudden slowing of the fetal heart rate which occurred between seventeen and nineteen hours before birth points to the onset of the abnormal mechanism at a specific time. The sudden onset of the heart block demanded a differential diagnosis between heart block and intra-uterine asphyxia. No anatomic abnormalities in the heart have been demonstrated, and the child is alive and healthy at 5 months of age.

4753 Broadway.

COLLES FRACTURE SPLINT

VERNON L. HART, M.D., MINNEAPOLIS

Numerous types of splints have been described for maintaining the reduction of a Colles fracture of the wrist. I have used many of them—nonpadded plaster, wooden, sugar tong plaster, anterior and posterior plaster molds, Schede's splint and commercial form-fit splints—but now regularly use the plaster splint to be described because it is easily applied, comfortable and efficient and it prevents complications. The two most distressing complications not infrequently observed are recurrence of radial deviation deformity of the distal fragment of the radius and hand and loss of function of the fingers and thumb because of adhesions and contractures of tendon sheaths and tendons. The plaster splint is applied over stockinet. Not more than two or three 4 inch plaster of paris rolls are used.

Fig. 1.—Ulnar view of plaster splint showing strip of plaster removed from the ulnar side of the entire splint, plaster removed from the ulnar styloid prominence, and complete flexion of interphalangeal and metacarpophalangeal joints.

No padding is used except for a small piece of felt over the radial or thumb site of the second metacarpal bone. Pressure at this point (fig. 2) is essential in order to maintain reduction of the distal radial fragment and hand in ulnar deviation. The original deformity is radial deviation of the distal radial fragment and hand and this often recurs after perfect reduction if immobilized in splints which do not maintain ulnar deviation.

After the plaster has hardened, a strip of plaster about one-half inch in width is removed from the ulnar side of the splint (fig. 1). This permits the splint to expand and accommodate the swelling which results from hemorrhage. Excessive swelling with edema will not occur if the fractured extremity is continuously elevated during the first several days after the injury.

A niche of plaster also is removed over the prominence of the ulnar styloid process to prevent pressure necrosis and pain.

The plaster is cut away so that complete flexion will be possible at the interphalangeal and metacarpophalangeal joints of the fingers (fig. 1). The second metacarpophalangeal joint will be slightly limited in flexion because of the extension of plaster along the thumb side of the second metacarpal.

Fig. 2.—Extensor view of splint which demonstrates the plaster pressure over the radial side of the second metacarpal bone to maintain reduction in ulnar deviation, the thumb window, plaster removed from ulnar styloid, and plaster extension to knuckles.

Plaster is next cut away to permit complete range of all motions of the thumb. The window at the thumb is extended proximally to remove plaster pressure and prevent pressure necrosis and pain at the base of the thumb or first carpometacarpal area (figs. 2 and 3). The plaster extends over the extensor surface of the metacarpals to the knuckles to maintain the position of the reduction in palmar flexion (fig. 2).

If x-ray studies demonstrate good reduction, the splint should be worn continually from four to six weeks. The patient is instructed to flex and extend all interphalangeal and metacarpophalangeal joints of the thumb and fingers completely and actively. Also the patient is instructed to rotate the thumb by touching the tip of the thumb to the end of each individual finger and to abduct and adduct the thumb and fingers. Supination and pronation of the forearm should be encouraged. The elbow and shoulder joints should be moved actively through the normal range of all motions. Besides these active subjective exercises the patient should be encouraged to perform active objective exercises by using the extremity for such activities as eating, dressing and combing the hair. Many patients may even return to their normal occupation after several days.

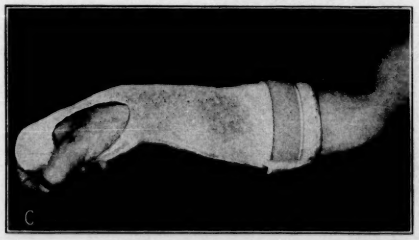


Fig. 3.—Radial view of splint which shows the thumb window and extension of plaster over the radial side of the second metacarpal bone.

Massage, light treatments and passive exercises should have no place in the therapeutic program of a fresh Colles fracture.

Therefore the splint which maintains the reduction of a Colles fracture should be one which will not be removed frequently for unnecessary physical therapy and will with comfort maintain continuous and uninterrupted immobilization until the fractured bones have united.

820 Medical Arts Building.

Special Articles

FOURTH ANNUAL SUMMARY OF FOURTH OF JULY INJURIES

DUE TO FIREWORKS AND EXPLOSIVES

SECOND SERIES

For each of the preceding three years the American Medical Association has compiled summaries of injuries[1] resulting from the celebration of the Fourth of July with fireworks. This report of injuries on the Fourth of July 1940 represents the fourth such report. They constitute a resumption of similar summaries which were published from 1903 to 1916 and were discontinued thereafter because of the reduction in the number of such injuries. The great increase in the fireworks injuries since then again has placed this problem among those of serious public importance.

DEATHS

In 1940 eight deaths were reported as directly due to the celebration of the Fourth of July with fireworks and other explosives. The distribution by states in comparison with figures for recent years is given in table 1. There has been a continuous decline in such deaths since the resumption of these reports in 1937. As in preceding years, several of the fatalities were due to burns resulting from the igniting of clothing from firecrackers. Two little girls, one in California, the other in New York, suffered fatal burns when their

TABLE 1.—*Deaths by State*

State	1940	1939	1938	1937
California	1	2	0	1
District of Columbia	1	0	0	0
Connecticut	0	0	1	0
Florida	0	1	0	1
Idaho	0	0	0	6
Illinois	0	1	1	0
Indiana	0	1	3	0
Iowa	1	0	0	0
Maine	2	0	0	0
Maryland	0	1	2	1
Massachusetts	0	2	0	2
Mississippi	0	0	1	0
New Jersey	1	1	0	1
New York	1	3	2	3
Ohio	0	0	1	1
Pennsylvania	0	0	6	0
Rhode Island	0	0	0	1
Texas	0	1	0	1
Utah	0	0	0	2
West Virginia	0	0	1	0
Wyoming	1	0	0	0
Totals	8	13	18	20

flimsy dresses caught on fire while they were playing with firecrackers. One young man in New Jersey was killed when a giant firecracker exploded inside his car and the machine crashed into a tree. One companion broke an arm, while the other suffered severe lacerations of the leg. All but two of the fatalities (in Iowa and New Jersey) occurred in states lacking in satisfactory antifireworks legislation.

TETANUS

In 1939 no cases of tetanus from fireworks injuries were reported, although there were 2 each in 1937 and 1938. There were 2 cases reported in 1940, 1 from Iowa and the other from California. Recovery occurred in both. The relative rarity of tetanus today doubtless can be ascribed to the almost universal use of tetanus antitoxin following injury rather than to lack of exposure.

SERIOUS INJURIES

Hospital questionnaires and newspaper clippings again record numerous serious and unusual injuries resulting from fireworks. A Pennsylvania lad lost a leg following the discharge of a fireworks "bomb" found in an unexploded form after a pyrotechnic display. A Virginia man suffered an injury to one kidney which required nephrectomy. Although in general there were not as many spectacular accidents recorded as in the preceding few years, the totals, as shown in table 2, are still high.

TABLE 2.—*Total Injuries by Type*

Injuries	1940	1939	1938	1937
Burns and lacerations	4,140	5,305	7,458	6,858
Loss of vision of one or both eyes	15	19	43	16
Injury to eye	199	158	281	294
Loss of finger, hand or other member	38	41	80	37
Internal injury, fracture or other serious accident	70	37	71	*
Total injuries	4,462	5,560	7,933	7,205

* Not classified.

INJURIES

Table 3 records the injuries from fireworks and other explosives in 1940 and, in parallel columns, the injuries for the preceding three years. As has been pointed out in previous reports, these figures do not take into consideration hospitals which failed to report on accidents treated in physicians' offices. The total, therefore, must obviously err on the side of underestimation.

As in most of the preceding years, New York State leads all others in the total number of injuries. Just prior to last summer's celebration, New York enacted antifireworks legislation. Like that which has been enacted in several other states, such legislation was not, however, to become effective until after the next Fourth of July. If the law is properly enforced, the results from that state in 1941 should show a material reduction in the number of injuries. New York was closely followed by Ohio, Illinois and Massachusetts in the total number of injuries, although Rhode Island led all other states in the number of injuries in comparison with the size of the population. California, Maryland, Minnesota, Missouri and Kansas still have relatively bad records. New Jersey, one of the first states to adopt satisfactory antifireworks legislation, has shown a steady rise in the number of injuries over the four years on record, thus indicating the need for more satisfactory administration. Obviously a law on the statute books is relatively useless unless enforcement is satisfactory. Among the states which have shown improvement Indiana is prominent, showing a reduction of injuries from 198 in 1939 to 2 in 1940. The record of Indiana is especially impressive, since it has gone from one of the worst states from the point of view of deaths and injuries to one of the very best. This is unquestionably

1. First Annual Summary of Fourth of July Injuries, Second Series, J. A. M. A. **109**: 1806 (Nov. 27) 1937; Second Annual Summary of Fourth of July Injuries Due to Fireworks and Explosives, ibid. **112**: 236 (Jan. 21) 1939; Third Annual Summary, ibid. **114**: 39 (Jan. 6) 1940.

due to the model law, which became effective since the preceding Fourth.

Baltimore this year leads all other large cities in the rate of injuries per hundred thousand of population, displacing Kansas City, Mo., which this year holds fifth place with the greatest reduction of any listed city.

TABLE 3.—*Injuries, by Type, Caused by the Celebration of the Fourth of July with Fireworks and Other Explosives*

State	1940						1939	1938	1937
	Burns and Lacerations	Loss of Vision of One or Both Eyes	Injury to Eye	Loss of Finger, Hand or Other Member	Internal Injury Fracture or Other Serious Accident	Total Injuries	Total Injuries	Total Injuries	Total Injuries
Alabama	25	0	0	0	0	25	17	15	7
Arizona	12	0	0	0	0	12	30	16	32
Arkansas	2	1	0	1	1	5	3	2	7
California	219	1	21	2	8	251	650	509	485
Colorado	10	0	1	1	0	12	10	21	119
Connecticut	47	0	0	1	0	48	201	125	104
Delaware	0	0	0	0	0	0	22	39	25
Washington, D. C.	67	0	0	0	1	68	57	31	78
Florida	42	0	1	0	2	45	62	29	23
Georgia	6	0	0	0	0	6	5	7	9
Idaho	6	0	1	0	0	7	7	5	52
Illinois	383	2	10	0	5	400	458	513	485
Indiana	2	0	0	0	0	2	198	346	278
Iowa	6	0	0	0	1	7	6	6	76
Kansas	136	0	9	2	0	147	61	74	93
Kentucky	12	0	0	0	1	13	6	11	61
Louisiana	3	0	0	1	0	4	12	2	12
Maine	43	0	3	0	0	46	59	75	67
Maryland	199	0	9	2	1	211	169	110	123
Massachusetts	275	1	24	6	8	314	333	467	376
Michigan	79	0	2	2	0	83	126	107	190
Minnesota	154	0	8	1	2	165	152	143	89
Mississippi	1	0	0	0	1	2	0	1	0
Missouri	143	0	5	3	4	155	357	553	510
Montana	19	0	1	0	3	23	38	30	50
Nebraska	21	1	4	2	2	30	17	14	49
Nevada	0	0	0	1	0	1	0	1	0
New Hampshire	29	1	3	1	2	36	25	32	40
New Jersey	147	0	8	1	2	158	112	88	72
New Mexico	1	0	2	0	0	3	5	5	1
New York	1,071	4	28	3	8	1,114	1,491	1,630	1,371
North Carolina	5	1	1	0	1	8	8	2	4
North Dakota	1	0	4	0	0	5	2	8	14
Ohio	426	0	25	4	6	461	337	585	353
Oklahoma	47	0	2	0	0	49	32	43	101
Oregon	42	1	2	1	1	47	27	39	45
Pennsylvania	47	0	7	2	2	58	85	1,702	991
Rhode Island	236	0	3	0	0	239	181	210	381
South Carolina	0	0	0	0	0	0	2	3	0
South Dakota	20	0	0	0	1	21	14	8	9
Tennessee	6	0	0	0	0	6	6	9	1
Texas	38	0	3	0	1	42	31	60	33
Utah	0	0	0	0	1	1	5	18	31
Vermont	4	1	1	0	0	6	1	2	20
Virginia	9	1	0	0	1	11	6	13	18
Washington	25	0	5	0	2	32	66	70	153
West Virginia	2	0	1	1	0	4	0	41	28
Wisconsin	55	0	1	0	1	57	66	117	92
Wyoming	2	0	4	0	0	6	2	6	10
Unknown	15	0	0	0	1	16	0	0	37
Totals	4,140	15	199	38	70	4,462	5,560	7,933	7,205

Los Angeles also had an improved record, resulting, no doubt, from the California restrictive legislation. Several of the smaller cities have even worse records than the large ones. Providence, R. I., leads with 138 injuries, or 54.54 per hundred thousand of population. This city is followed by Lynn, Mass., Youngstown, Ohio, and Kansas City, Kan., with 48, 71 and 23 injuries, giving rates of 46.91, 41.76 and 18.87 per hundred thousand of population, respectively.

This year hospitals were especially requested to list injuries from cap pistols separately, and these are given in table 5.

COMMENT

Again the effectiveness of adequate state legislation in reducing the toll of fireworks injuries has been demonstrated and is particularly well illustrated this year in the case of Indiana. In spite of repeated emphasis in these reports on the danger of postponing the effective date of legislative enactment, New York, which passed such legislation in advance of the Fourth, delayed enforcement until next year: 1,114 accidents were reported from that state. Maryland has had a repeatedly bad record but has not yet enacted satisfactory legislation: this year 211 injuries were reported from that small state. With the exception of most of the Southern states, which do not celebrate the Fourth of July extensively with fireworks, there are few exceptions to the rule that only those states which have enacted and enforced statewide laws have shown evidence of satisfactory control. In spite of satisfactory legislation in New Jersey, the toll of injuries has been

TABLE 4.—*Injuries in Principal Cities*

City	1940		1939		1938		1937	
	Injuries	Rate per 100,000	Injuries	Rate per 100,000	Injuries	Rate per 100,000	Injuries	Rate per 100,000
Baltimore	185	22.98	135	16.75	68	8.43	56	6.95
St. Paul	55	20.25	58	21.35	..	....	..	....
Jersey City, N. J.	63	19.89	51	16.10	..	....	..	....
Washington, D. C.	68	13.97	57	11.71	..	....	..	....
Kansas City, Mo.	55	13.76	243	60.83	..	....	..	....
Cincinnati	62	13.74	31	6.87	..	....	..	....
Los Angeles	124	10.02	258	20.91	180	14.59	45	3.63
Boston	76	9.73	71	9.01	..	....	..	....
New York and Brooklyn	631	9.10	828	11.85	1,008	14.43	524	7.56
Minneapolis	41	8.83	46	9.90	..	....	..	....
Chicago	253	7.49	226	6.69	176	5.21	225	6.66
Cleveland	64	7.11	42	4.66	129	14.32	64	7.11

TABLE 5.—*Cap Pistol Injuries*

State	Burns	Gunpowder Infections	Lacerations and Puncture Wounds	Eye Injuries	Mutilations	Total
California	1	..	..	..	..	1
Connecticut	2	1	2	..	..	5
Illinois	3	..	..	..	..	3
Iowa	..	1	..	..	..	1
Kentucky	2	..	..	..	..	2
Maine	2	..	..	..	..	2
Maryland	1	..	..	..	..	1
Massachusetts	..	..	..	1	..	1
Minnesota	2	..	..	..	..	2
Missouri	2	..	..	..	..	2
New Hampshire	1	..	..	..	..	1
New Jersey	16	..	..	..	1	17
New Mexico	1	..	..	..	..	1
New York	6	..	..	1	..	7
Ohio	3	..	..	1	..	4
Oregon	1	..	..	..	..	1
Pennsylvania	12	..	1	1	1	15
Rhode Island	2	..	..	..	..	2
South Dakota	2	..	..	..	..	2
Texas	2	..	..	..	..	2
Vermont	..	..	1	..	..	1
Wisconsin	1	..	..	..	..	1
Totals	62	2	4	4	2	74

rising consistently there and the need for more satisfactory enforcement is obvious. The injuries and deaths still resulting from this unnecessary cause clearly illustrate the need for additional legislation and consistent enforcement.

GLANDULAR PHYSIOLOGY AND THERAPY

LACTOGENIC AND MAMMOGENIC HORMONES

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Investigations of the past twelve years provide much new information concerning the regulation of growth and of secretion in the mammary glands. Both growth and secretion are controlled mainly by hormones, but quite different hormones are involved in these two wholly distinct sets of processes. The anterior lobe of the pituitary exercises a direct control (through its lactogenic hormone, prolactin) over milk secretion; in addition it exercises an indirect control (through estrogen, progesterone and possibly other sterols) and perhaps also a direct control (through a mammogenic pituitary hormone) over the development and growth of the mammary glands.

THE LACTOGENIC HORMONE

The Lactogenic Response.—Stricker and Grüter demonstrated in 1928-1929 that a factor or combination of factors directly essential to lactation is produced by the anterior lobe of the pituitary. Their results were confirmed first by Corner in 1930 and thereafter extended to various species by Nelson and Pfiffner, Turner and Gardner, Asdell and others. Indeed both mammary proliferation and lactation were observed to follow the administration of crude pituitary extracts in females with intact ovaries by Parkes in 1929 (rabbits), by Putnam, Benedict and Teel (bitches) and by Evans and Simpson (rats), but this effect either was or could then be attributed to pituitary influence on hormone production in the ovary. A related response, the enlargement of the crop sacs of pigeons with formation of "crop milk," was reported in 1931 by Riddle and Braucher. All these results were obtained with simple glandular extracts—mixtures of various pituitary products—and provided no indication of the identity of the hormone or hormones that excited this response.

Isolation and Identification of the Hormone.—The individuality of the hormone that excites lactation was established in 1932-1933 through its isolation and study by Riddle, Bates and Dykshorn,[1] who definitely associated it with lactogenic and crop-stimulating functions and called it prolactin. Confirmation of its individuality and lactogenic function was soon supplied by Catchpole and Lyons [2] and Lyons and other associates,[3] who called the hormone mammotropin, and by Gardner and Turner,[4] who also fully described the mammary changes accompanying its lactogenic action in the rabbit. Gardner and Turner called this hormone galactin.

Occurrence.—The hormone is probably present in the hypophyses of all vertebrates but is more plentiful in some species and at certain stages of the life cycle than others. Beef and sheep glands usually yield 30 to 40 international units per gram of fresh tissue, while pork glands contain much less.[5] Pituitaries of fetal calves were once reported [6] to contain much more prolactin (78 + units) than the glands of adult or pregnant cows (38-44 units), but a later report [7] stated these values in essentially the reverse order. In the study represented in the latter report a higher concentration of hormone was found in glands from dairy cattle than in those from beef cattle, and in both studies a somewhat higher concentration was found in glands from pregnant (or lactating) cows than in those of heifers. There is evidence that prolactin is formed in the eosinophilic cells [8] and that administration of estrogen increases the amount of it (stored?) in the rat gland.[9] Small amounts have been found repeatedly in postpartum human urine (also in urine of normal men and in that of infants during the first week) since this was first reported by Lyons and Page,[10] who stated that the amount excreted daily is equal to that found in one beef pituitary. It is alleged that two peaks of excretion occur within the normal cycle of the female sex: during menstruation and during ovulation.[11] Positive tests were reported for human serum [12] and for young (not for mature) placentas [13] and notable quantities from cystic human breasts.[14] Hoffmann [15] found less than the expected amounts of prolactin in the urine of seven of eight parturient women whose secretion of milk was subnormal. Rabald and Voss [16] reported recovery of a prolactin-like substance from the livers of healthy cattle and hogs but not from horse liver.

Preparation and Assay.—Currently used methods of preparing [17] prolactin from pituitary tissue involve its initial extraction in acid or alkaline medium (aqueous or 60 per cent alcohol [ethyl alcohol], or acid acetone), its isoelectric precipitation in an aqueous medium and repeated washing of this precipitate. Comparisons of the various methods are available.[18] Current methods of assaying prolactin were surveyed by McShan and Turner,[19] Bergman and Turner,[20] and Bates; [21] crop sacs of

From the Carnegie Institution of Washington, Station for Experimental Evolution.

1. (a) Riddle, Oscar; Bates, R. W., and Dykshorn, S. W.: A New Hormone of the Anterior Pituitary, Proc. Soc. Exper. Biol. & Med. **29:** 1211 (June) 1932; (b) Prolactin, a New and Third Hormone of the Anterior Pituitary, Anat. Rec. (supp.) **54:** 25 (Nov.) 1932; (c) The Preparation, Identification and Assay of Prolactin—a Hormone of the Anterior Pituitary, Am. J. Physiol. **105:** 191 (July) 1933.

2. Catchpole, H. R., and Lyons, W. R.: The Lactation Hormone of the Hypophysis, Anat. Rec. (supp.) **55:** 49 (March) 1933.

3. Lyons, W. R., and Catchpole, H. R.: Assay with the Guinea Pig of the Lactogenic Hypophysial Hormone, Proc. Soc. Exper. Biol. & Med. **31:** 299 (Nov.) 1933. Catchpole, H. R.; Lyons, W. R., and Regan, W. M.: Induction of Lactation in Heifers with the Hypophysial Lactogenic Hormone, ibid. p. 301. Lyons, W. R.; Chaikoff, I. L., and Reichert, F. L.: Experiments with Hypophysial Lactogenic Hormone on Normal, Ovariectomized and Hypophysectomized Dogs, ibid., p. 303. Lyons, W. R., and Catchpole, H. R.: Availability of the Rabbit for Assay of the Hypophysial Lactogenic Hormone, ibid., p. 305.

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9. Reece, R. P., and Turner, C. W.: Experimentally Altering Galactin Content of the Rat Pituitary, Proc. Soc. Exper. Biol. & Med. **36:** 283 (April) 1937.

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12. Tesauro, G.: Contributo allo studio dell'ormone galattogeno, Pediatria **44:** 665 (Aug.) 1936.

13. Ehrhardt, Karl: Ueber das Laktationshormon des Hypophysenvorderlappen, München. med. Wchnschr. **29:** 1163 (July 17) 1936.

14. Geschickter, C. F., and Lewis, Dean: Lactogenic Substance in the Human Breast, Arch. Surg. **32:** 598 (April) 1936.

15. Hoffmann, Friedrich: Ueber die hypophysäre Hypogalaktie, Zentralbl. f. Gynäk. **61:** 35 (Jan. 2) 1937.

16. Rabald, E., and Voss, H. E.: Ueber Vorkommen und Eigenschaften des Laktationshormons, Ztschr. f. physiol. Chem. **261:** 71, 1939.

17. Bates and Riddle,[5] McShan and Turner,[19] Lyons,[22]

18. Riddle, Oscar, and Bates, R. W.: The Preparation, Assay and Actions of Lactogenic Hormone, in Allen, Edgar; Danforth, C. H., and Doisy, E. A.: Sex and Internal Secretions, ed. 2, Baltimore, Williams & Wilkins Company, 1939, chap. 20, p. 1088. Bergman and Turner.[20]

19. McShan, W. H., and Turner, C. W.: Further Purification of Galactin, the Lactogenic Hormone, Proc. Soc. Exper. Biol. & Med. **32:** 1655 (June) 1935.

20. Bergman, A. J., and Turner, C. W.: Comparison of Methods of Extraction of the Lactogenic Hormone, J. Biol. Chem. **118:** 247 (March) 1937.

21. Bates, R. W.: Methods for the Assay of Prolactin, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1937, vol. 5, p. 191.

pigeons (macro and micro tests available) or of lactation in pseudopregnant rabbits. The micro test in pigeons is said to be sensitive to 0.01 microgram of lactogenic hormone.[22]

For assay of this hormone in urine (or serum) Lyons [22] now injects unconcentrated urine intradermally (micro test) over the crop sacs of pigeons 1 month old. Four daily injections (0.05 to 0.5 cc.) are made at five sites on each crop gland (feathers removed), with necropsy twenty-four hours after the last injection. After stripping away the muscle and the inflammatory exudate which always results from the toxic substances in the urine and which masks minimal reactions, the crop wall is inspected against good light for stimulation at the sites of injection. By using varying quantities on a few birds, a standard or minimal effective dose of the urine (preserved with hexylresorcinol) is determined.

Four quite different macro units ("pigeon units") now confuse the literature, but a practical solution is at hand. A standard preparation of the lactogenic (crop gland-stimulating) substance—to be distributed on behalf of the League of Nations Health Organization—is available from the National Institute for Medical Research, Hampstead, London, England. Samples made in different laboratories were combined to form this standard preparation, and it was decided that "agreement shall be reached among the members of the Conference as to the activity of the standard preparation in 'Riddle-Bates units' per milligramme, and that the international unit shall be thus defined in terms of the standard preparation." [23]

Properties.—Prolactin is insoluble in all fat solvents. It is soluble in water except in the isoelectric region *p*H 5-6 and in strongly acid solution, < 0.5. When made acid to the isoelectric point, the extract containing prolactin is precipitated by the usual protein precipitants—e. g., by tannic, phosphotungstic, flavianic and trichloroacetic acids and by trinitrophenol. It may be salted out with sodium (or ammonium) sulfate or sodium chloride, the amount required depending on the *p*H. It is also precipitated by basic salts of heavy metals at or near *p*H 7.[24] It is rapidly inactivated by trypsin [25] and pepsin.[26] Salt-free solutions at *p*H 8 withstand boiling for one hour with little loss; under other conditions the prolactin may be rapidly destroyed.[27] A crystalline protein with fairly high lactogenic activity was extensively studied by White, Catchpole and Long [28] and found to have the following elemental composition in percentage: carbon 51.11, hydrogen 6.76, nitrogen 14.38, sulfur 1.77, phosphorus 0. In their better preparations of prolactin Bates and Riddle [29] found roughly 2 per cent each of tyrosine, cystine and tryptophan. Tests indicated that free amino groups in prolactin are essential to its activity.[30] More advance has been made in the chemical study of prolactin than in that of any other anterior pituitary hormone.

Applications and Actions.—For increasing the milk yield of domestic animals after lactation has been established or during declining lactation, prolactin has sometimes [31] but not always proved efficacious; likewise, from whole pituitary extracts both success and failure are recorded; [32] still other glandular products (notably thyroxin) [33] have sometimes proved of equal or of greater effectiveness for these unusual requirements. Again, the adrenal cortex—perhaps incident to its regulation of fluid and salts or to the production of sterols supporting mammary growth—seems to contribute something essential to the maintenance of milk flow or even to the initiation of this function in some species,[34] though apparently not in the dog.[35] Similarly, hypophysectomy, thyroidectomy or hysterectomy may markedly affect lactation. Finally, estrogen, though certainly helpful in the preparation of mammary tissue, becomes for one true action of prolactin an agent decidedly adverse to milk yield after lactation has been established.[36]

Since it is thus obvious that so much of the organism —assimilative, endocrine and neural—becomes involved in the initiation, augmentation and maintenance of lactation, the term "lactogenic hormone" is equivocal and its use often a serious error; others (not ourselves) have rather generally ventured to employ this term as an alternative designation for that hormone which was found to initiate milk secretion in prepared mammary tissue and which after its isolation and establishment as an entity was called prolactin. Lactogenesis involves several hormones and many other factors; prolactin is a specific substance. Only full recognition of this distinction, along with awareness of other actions of prolactin, is likely to lead to satisfactory clinical use of this substance.

Clinical use of prolactin hitherto has been restricted largely to postpartum women with deficient lactation. In the earliest tests [37] twenty-nine women whose lactation had failed to develop adequately by the sixth to the ninth day were then given one or two intramuscular injections of prolactin, totaling 75 to 400 units. This dosage (highest, 200 units per injection) was well tolerated. In twenty-five of these women the daily milk yield increased by from 50 to 400 Gm. within three to nine days; there were four or five definite failures, in all of which the total dose used was only 100 to 150 units. In eight other women, whose milk secretion was or presumably would become normal, dosage for a single day with 100 to 400 units at one to fifteen days post partum probably induced no change. Werner [38] noted that eight castrates whose breasts were variously prepared (or unprepared) by previous estrogenic treatment did not lactate after intramuscular injection of 200 units of prolactin daily

22. Lyons, W. R.: Preparation and Assay of Mammotropin, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1937, vol. 5, p. 198.

23. Report of the Third International Conference on the Standardization of Hormone: IV. Consideration of the Lactogenic (Crop-Gland-Stimulating) Substance of the Anterior Lobe of the Pituitary Gland ("Prolactin," "Galactin," Mammotropin), Bull. Health Org. League of Nations **7:** 892 (Oct.) 1938.

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28. White, Abraham; Catchpole, H. R., and Long, C. N. H.: A Crystalline Protein with High Lactogenic Activity, Science **86:** 82 (July 23) 1937.

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35. Kendall, E. C.; Mason, H. L.; Myers, C. S., and Allers, W. D.: Physiological and Chemical Investigation of the Suprarenal Cortex, J. Biol. Chem. **114:** lvii (May) 1936; personal communication to the author.

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38. Werner, A. A.: Experiment to Produce Lactation in Castrate Women, Endocrinology **19:** 144 (March-April) 1935.

for one to fourteen days; severe local and systemic reactions were produced in three of these women (two others reported on later). Evans [39] briefly reported seven successful tests with total doses of from 1,000 to 2,250 units. Hoffmann [40] noted that a total dose of 200 to 250 units given in two days may or may not increase the milk yield.

Two recent critical studies on the effects of twice-daily injections during two to four days, beginning on the sixth or seventh day post partum, led to somewhat different conclusions, though there were several obvious failures in both series of tests. Ross,[41] using intramuscular injections during two days, gave a total dose of 400 units to nine patients and 1,000 units to twelve others. Only the larger dose appeared to result in an appreciable increase in milk secretion, and only this dose produced any adverse local reactions; the latter involved redness and indurations varying in diameter from 2 to 15 cm., and a rise in temperature to 100 to 102 F. for two to six days. Considered of special significance was the observation that a higher proportion of the mothers given the larger dose were able to nurse their infants after discharge from the hospital. Stewart and Pratt,[42] giving a subcutaneous injection of 1,000 units daily from the sixth to the ninth postpartum day inclusive, got no significant increase in milk secretion from a group of fourteen patients whose secretion was less than 250 cc. on the fifth day. A similar group of ten mothers served as controls, and after leaving the hospital their nursing record was not significantly different from that of the group given prolactin. Stewart and Pratt conclude that the action of prolactin in animals is not analogous to that in women.

The most recent study is also the most complete and informative. Kenny and King [43] treated forty-three women with prolactin for deficient lactation, beginning at different stages up to the third month post partum; forty-three other women, to whom other "galactogogues" were given or on whom routine methods of encouraging lactation were practiced, served as controls. In 74 per cent of the treated women and in only 21 per cent of the controls lactation became sufficient for the whole need of the baby until weaning at the sixth to the seventh month. The complete failures included 19 per cent of the treated women and 63 per cent of the controls. The total dose of prolactin was 900 units, which was given intramuscularly at the rate of two injections a day for five days, as follows: on the first and second days 300 units a day, on the third and fourth days 120 units a day and on the fifth day 60 units. No local or systemic ill effects were observed. The milk produced was of normal composition and quality. They recommended that treatment begin early in order that efficient nursing might be established before discharge from the hospital.

Other actions of prolactin have been reported from animal experimentation, though appropriate clinical applications have not yet been published. In adult birds prolactin has powerful antigonad action, made evident by extremely rapid and nearly complete atrophy of the testes [44] and by speedy inactivation and regression of the ovary.[45] In adult male rats 10 to 20 units of prolactin daily for eight to fifteen days does not decrease the weight of the testes.[46] In female mice [47] and rats [48] dosage with prolactin stops estrous cycles. Small amounts of luteinizing substance also stop the cycles of mice, and since luteinizing substance is a contaminant of many prolactin preparations it has been suggested [49] that this action on the cycles of rodents is exercised by the luteinizing substance. Though it is clear that prolactin is, and luteinizing substance is not, effectively antigonad in birds, this action of prolactin is still uncertain in mammals.

Prolactin seems to be specifically involved in the onset or production of broodiness in the fowl,[50] the maternal or parental instinct in rats [51] and nesting behavior in fish.[52] Other anterior pituitary extracts, the urinary luteinizing substance, estrone (theelin), progesterone and extract of adrenal cortex all seem ineffective or inhibitory in the fowl, though phenol is active in fish, and pituitary luteinizing extract, intermedin, progesterone, desoxycorticosterone acetate and phenol are all fairly effective in rats.

Prolactin has marked calorigenic action in pigeons—normal, hypophysectomized or thyroidectomized—and its synergistic action with thyrotropin on heat production has been reported in normal doves.[53] The relation of prolactin to carbohydrate and fat metabolism is an important but still unsettled problem.[54] Splanchnomegaly exhibited in the liver, pancreas and intestine of the pigeon is associated with the action of prolactin.[55] Body weight and appetite are especially increased by prolactin in pigeons, and favorable effects of this substance on the growth of the dwarf mouse—with a synergistic effect on growth when prolactin is administered together with thyrotropin—have been reported.[56]

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Large doses of ox pituitary prolactin (probably not entirely free from serum protein) injected daily into adult rabbits or young female monkeys for eighteen or more weeks resulted in the production of antiserums capable of inhibiting the growth response in the crop sac of the pigeon and probably of reducing milk secretion in lactating mice.[57] Preparations of prolactin from ox and sheep glands, apparently free from serum protein, were found to be antigenically indistinguishable, and the serum of rabbits given injections of prolactin from either source usually partly inhibited prolactin action on crop sacs.[58]

MAMMOGENIC HORMONES

The Mammogenic Response.—Numerous old and new studies clearly prove that hormones of the ovary play a part in the growth of the mammary gland—in most species an estrogen induces (directly or indirectly) duct growth, and an estrogen plus progesterone induces lobule-alveolar development. Androgens, too, were later proved capable of replacing estrogens in the induction of growth in the mammary parenchyma. Still more recently desoxycorticosterone acetate and some phenanthrene and stilbene compounds not now known to occur in the body are reported to cause duct development in normal and castrate males of the species studied.

In hypophysectomized animals, however, the use of estrogens or androgens to develop mammary tissue has usually, though apparently not always, resulted in failure. Such failures together with the recovery of potent lipoid extracts from the anterior lobes of pituitary glands which have been recently subjected to ovarian hormones—and other related facts—lead some investigators to believe that the pituitary gland secretes, in addition to its various hormones of protein nature, other (alcohol-ether soluble) hormone(s) with specific ability to induce mammary growth. In this review one needs to consider only literature bearing on (1) the question of whether estrogens, androgens and available phenanthrenes act directly or indirectly on mammary tissue and (2) the intimately related question of the elaboration of specific mammogenic hormone(s) by the pituitary.

Direct or Indirect Action of Sterols.—Duct development was reported in 4 of 5 hypophysectomized male rats treated for fourteen days with 50 mouse units of estrone twice daily [59] and in mammary glands transplanted into similar rats.[60] Rapid mammary involution was observed in rats after hypophysectomy on the sixth day of lactation despite the injection of 100 micrograms of estrone daily; the conclusion was drawn that the pituitary is necessary for the action of estrone on the mammary gland.[61] Mammary involution would be expected to follow the withdrawal of prolactin and the generally adverse effects of hypophysectomy, and it was later reported [62] that the involution of the lobule-alveolar system of such rats is not rapid but requires at least as long as does its development. Houssay [63] observed teat and mammary enlargement in a male hypophysectomized dog given 10,000 international units of estrone daily for fifty-four days.

Estrone plus progestin was observed to cause further mammary development in hypophysectomized castrate rats than did estrone alone,[64] and the same was observed in guinea pigs similarly operated on.[65] In 4 hypophysectomized, ovariectomized rabbits given daily for fifteen days injections of 25 rat units of estradiol benzoate and 4 rabbit units of progestin, mammary development approximately equal to that in rabbits incompletely operated on or not operated on was reported.[66] Corner [67] had shown much earlier that in castrate rabbits with intact hypophyses progestin alone is without effect, and others [68] had observed that estrone plus progestin did cause development of the mammaries of such rabbits.

Later studies (since 1935) with estrogens on pituitaryless animals have more often given negative results on mammary growth, but the significance of these failures has been interpreted variously. Mammary growth in such rats was not stimulated by 25 to 500 international units of estradiol benzoate daily for fifteen to forty-five days,[69] by 20 to 100 units of estrone for twenty to twenty-five days [70] and only slightly after estrone,[71] even when the general condition of the rat was sustained with pituitary extract.[72] Selye and Collip [72] therefore reaffirmed the view that this action of estrone must be through the pituitary. Astwood and his associates [73] emphasized the great importance of reduced nutrition incident to hypophysectomy. They observed mammary regression in normal rats on restricted diet during fourteen days, although 5 micrograms of estrone was injected daily. Likewise, in hypophysectomized rats the duct system regressed under estrone dosage, and the authors concluded that such failures provide insufficient evidence that mammary growth is mediated by the pituitary. Other failures of estrogens to support or increase mammary growth in pituitaryless animals were observed in guinea pigs, mice, rabbits, cats and ground squirrels.[74] Herold and Effkemann [75] reported no effect of estrogen in normal male and castrate female rats after severing the nerve connection between the pituitary and the midbrain and suggested that estrone acts by way of the diencephalon

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75. Herold, L., and Effkemann, G.: Abhängigkeit der Follikelhormonwirkung auf die Brustdrüse von der nervösen Verbindung der Hypophyse zum Zwischenhirn, Klin. Wchnschr. **18:** 455 (April 1) 1939.

from which impulses reach the pituitary and cause it to secrete a mammary growth factor.

When the pituitary was removed during pregnancy, the effects on mammary growth were unexpected and important. In rats operated on during the second week mammary growth was unaffected, and the usual accumulation of metabolic products in the lobular cells occurred.[76] In guinea pigs operated on at the fortieth day, with mammaries examined nine to twelve days later, a condition resembling that of normal glands at parturition was found.[77] In mice it was observed that even after digital abortion of fetuses and hypophysectomy on the twelfth day normal mammary changes occurred if the placentas had been retained;[78] the presence of the ovaries had earlier been found unessential for mammary growth at this period.[79] These results recall earlier evidence for an influence of the placenta on both mammary growth and secretion in animals with intact pituitaries.[80] That this influence may result from the secretion of an estrogen by the placenta, or otherwise, is obvious.

Testosterone and other androgens have been observed to cause mammary development in normal or ovariectomized rats.[81] In hypophysectomized rats little or nothing more than nipple growth is obtained.[82] In young male mice, not unoperated on, and in castrated male mice weighing from 15 to 25 Gm., the development of the mammary glands was accomplished with a wide variety of estrogens and androgens and with desoxycorticosterone acetate.[83] This result with the last named substance has special importance because (1) it adds the adrenal cortex to the few possible sources of mammogenic stimulation, (2) these cortical products are heat labile (in contrast with many estrogens) and more soluble in fat solvents, (3) such products are probably released from the cortex in increased amounts by estrone dosage in normal rats and pigeons but not or to a less extent after hypophysectomy,[84] (4) desoxycorticosterone (the only adrenal derivative hitherto tested) was observed in the study cited to have greater mammogenic potency per milligram than either of the five androgenic substances tested and (5) mice of just this type are used for assay of the mammogenic activity of the pituitary tissues and extracts to be described in the following section.

Mammogenic Potency of Pituitary Tissues and Extracts.—Implantation of pituitary tissue was followed by no appreciable mammary development in many tests made on rats.[85] In other tests, positive results in both ducts and lobules were secured on hypophysectomized male castrate and noncastrate guinea pigs following implantation of tissue from rats previously treated with estrogen.[86] In pituitaryless male and female guinea pigs a few tests with an extract of adrenal cortex (eschatin) alone or in combination with an estrogen (not named) indicated no mammary growth. Some further tests were reported, together with citations from the literature, indicating the ineffectiveness of thyroxin and of the recognized pituitary substances.[70] In a later study immature ovariectomized rats and spayed rabbits showed complete mammary development following implantation during twenty-five to thirty days of fresh (or acetone-dried) anterior pituitary tissue from pregnant cows.[87] In view of these results a new pituitary principle promoting growth in the mammary gland was postulated by Gomez and Turner and called "mammogenic hormone," or mammogen.

Nelson[88] reported that the mammary development of hypophysectomized immature female rats in which pituitaries from estrogen-treated rats of either sex had been implanted did not exceed or even equal that which followed implantation of normal rat pituitaries. He also announced his failure to confirm the claim of the existence of a specific "mammogenic hormone." Repeating this study, Reece and Leonard[89] also found no difference in the potency of pituitaries from untreated and estrogen-treated donors, but they noted that implanted glands of both types gave evidence of some growth when the test animals were compared with their untreated hypophysectomized control.

Albino mice were found to respond to pituitary implants and were considered most suitable for assay of mammogen.[90] The technic of this assay of the factor promoting duct growth involves the daily subcutaneous injection of macerated fresh anterior lobe tissue from pregnant cows or of mammogen-containing extracts for six days with autopsy on the seventh. The mouse unit is defined as the amount of tissue or extract required (per mouse) to produce definite signs of duct development in one or more glands of 50 ± 10 per cent of ten or more male albino mice weighing 15 to 25 Gm.[91] With this technic the mammogen content of the pituitaries from pregnant cows was found greatest at one hundred and fifty days; that of the dairy cow was greater than that of the pregnant beef cow; that of beef heifers with corpora lutea was 40 to 60 per cent greater than that of pregnant beef cows at the one hundred and fifty day peak; steer, bull and fetal

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91. Lewis, Turner and Gomez.[90] Lewis and Turner.[90]

pituitaries showed appreciable amounts of mammogen.[92] The authors suggested that estrogens lead to the production of a pituitary factor promoting duct growth, progesterone to a factor promoting lobule proliferation.

Lewis and Turner [93] observed that acetone and ether drying of prehypophysial tissue resulted in a loss of 60 per cent of its mammogen content. Extraction of the tissue with several volumes of hot ether–alcohol (1:3) resulted in a preparation (oily residue) containing 1 unit per 3 to 4 mg. and including practically 100 per cent of the potency of the fresh tissue. In their most recent publication [92] they have stated that their most potent preparation, tested in fourteen mice, gave positive results in 79 per cent at a dosage of 0.25 mg. per mouse. The estrogen content of some preparations was measured and considered far too low to have caused the mammary growth observed. The fact that fresh pituitary tissue containing mammogen caused both duct development and lobule hyperplasia, though the lipoid extracts cause only duct development, was regarded as evidence that the lipoid solvent separates a duct growth factor from a lobule growth factor.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

LIVER AND STOMACH PREPARATIONS (See New and Nonofficial Remedies, 1940, p. 320).

SOLUTIONS FOR PARENTERAL ADMINISTRATION

TEN CC. SOLUTION LIVER EXTRACT PARENTERAL-LEDERLE.—A sterile aqueous solution containing the nitrogenous nonprotein fraction G of Cohn et al. obtained from fresh mammalian liver, preserved with 0.5 per cent of phenol. The daily parenteral administration of 0.3 cc. has been found to produce the standard reticulocyte response defined as 1 U. S. P. unit (injectable) when assayed in cases of pernicious anemia as required by the Council.

Actions and Uses.—Solution liver extract parenteral-Lederle is proposed for intramuscular injection in the treatment of pernicious anemia. (See general article Liver and Stomach Preparations, New and Nonofficial Remedies, 1940, p. 320.)

Dosage.—To insure optimum dosage for cases of pernicious anemia in relapse it is advisable to make an injection of 5 cc. each day for three or four successive days. In a series of cases in which remissions have been thus initiated by the use of solution liver extract parenteral-Lederle there is evidence that injections of 5 cc. every two weeks (or 1 cc. twice weekly if low unit, more frequent dosage is preferred) provide sufficient active material to complete the remission and maintain a satisfactory blood picture. In complicated cases and those with extensive neurologic involvement, the optimum dosage may be much larger and must be determined for each patient.

Manufactured by the Lederle Laboratories, Inc., Pearl River, N. Y.

Vials Solution Liver Extract Parenteral-Lederle, 10 cc.

Concentrated solution liver extract parenteral-Lederle is prepared as follows: A mixture of finely ground liver and water is acidified to the isoelectric point, *p*H 5.0-5.4. After partial coagulation of the liver proteins is effected by heating to 75-85 C. the pulp is separated by filtration, centrifugation or pressing and the aqueous filtrate is concentrated in vacuo to the consistency of a thin syrup. By careful fractional precipitation with large volumes of alcohol at low temperatures (4 C.) much inactive material (proteins) is precipitated and subsequently discarded. The alcoholic filtrate is concentrated in vacuo and sufficient alcohol added to precipitate the active material (fraction G) of Cohn et al. (Proceedings of the American Society of Biological Chemistry, *J. Biol. Chem.* **74**: lxix [July] 1927). The washed precipitate generally known as "Cohn's fraction G," commonly obtained as a hygroscopic, brownish powder, in addition to the active antianemic factor, contains much inert matter. In order to obtain a concentrate of the active factor as free as possible from inert substances, the solution containing the fraction G of Cohn is treated with a special activated carbon.

After filtering off the carbon the solution containing the active principle is concentrated in vacuo to a point where approximately 2.7 cc. represents the active material obtained from 100 Gm. of liver. Subsequently sufficient phenol is added to make 0.5 per cent in the finished product; volume is adjusted and the solution is sterilized by Berkefeld filtration.

SOLUTIONS FOR PARENTERAL ADMINISTRATION
(See New and Nonofficial Remedies, 1940, p. 327)

PARENTERAL SOLUTION OF LIVER, 5 U. S. P. UNITS PER CC.-NATIONAL DRUG CO.—A sterile aqueous, clear, dark brown solution containing all of the fraction G of the liver extract (Cohn), preserved with 0.5 per cent of phenol. The daily parenteral administration of 0.2 cc. has been found to produce the standard reticulocyte response defined as 1 U. S. P. unit (injectable) when assayed in cases of pernicious anemia as required by the Council.

Actions and Uses.—Parenteral solution of liver-National Drug Company is proposed for intramuscular injection in the treatment of pernicious anemia. See the general article Liver and Stomach Preparations (New and Nonofficial Remedies, 1940, p. 320).

Dosage.—Daily intramuscular injections of 1 cc. for three to four days may be sufficient for the average case. For more severe cases the doses may be raised to from 2 cc. to 4 cc. It is desirable to give at least 20 units (4 cc.) on the first and second days, but it may be advisable in the case of patients who are to receive the larger doses to divide the dose and give one half of the amount into each gluteal muscle. After seven days' interval, 10 units (2.0 cc.) may be administered at weekly intervals. The dosage of course will vary with the individual patient, depending on the degree of complications.

Distributed by the National Drug Company, Philadelphia.

Ampul-Vial Parenteral Solution of Liver-National Drug Company, 10 cc. (5 U. S. P. Injectable Units per cc.).

Parenteral solution of liver-National Drug Company in bulk is passed through a Berkefeld filter into a large sterile container and then it is tested for sterility. If the solution is found to be sterile, it is injected intracutaneously in rabbits and subcutaneously in guinea pigs. Rabbits are tested for necrosis; guinea pigs are checked for edema and general reactions. When these tests show that the material is free from reactions, the solution is filled aseptically into sterile 10 cc. ampul vials. After filling, the material is tested for sterility. Ten containers are selected from the entire lot and each is tested for sterility. If any of these ten tested containers shows growth, ten more bottles are tested. If growth appears on retesting these new ten ampul vials, the entire lot is then reprocessed.

PARENTERAL SOLUTION OF LIVER, 10 U. S. P. UNITS PER CC.-NATIONAL DRUG CO.—A sterile aqueous, clear, dark brown solution containing all of the fraction G of the liver extract (Cohn), preserved with 0.5 per cent of phenol. The daily parenteral administration of 0.1 cc. has been found to produce the standard reticulocyte response defined as 1 U. S. P. unit (injectable) when assayed in cases of pernicious anemia as required by the Council.

Actions and Uses.—Parenteral solution of liver-National Drug Company is proposed for intramuscular injection in the treatment of pernicious anemia. See the general article Liver and Stomach Preparations (New and Nonofficial Remedies, 1940, p. 320).

Dosage.—Daily intramuscular injection of 0.5 cc. for three to four days may be sufficient for the average case. For more severe cases the doses may be raised to from 2 to 4 cc. It is desirable to give at least 20 units (2 cc.) on the first and second days, but it may be advisable in the case of patients who are to receive the larger doses to divide the dose and give one half of the amount into each gluteal muscle. After seven days' interval, 10 units (1.0 cc.) may be administered at weekly intervals. The dosage of course will vary with the individual patient, depending on the degree of complications.

Distributed by the National Drug Company, Philadelphia.

Ampul-Vial Parenteral Solution of Liver-National Drug Company, 10 cc. (10 U. S. P. Injectable Units per cc.).

Parenteral solution of liver-National Drug Company, in bulk as purchased is passed through a Berkefeld filter into a large sterile container and then it is tested for sterility. If the solution is found to be sterile, it is injected intracutaneously in rabbits and subcutaneously in guinea pigs. Rabbits are tested for necrosis; guinea pigs are checked for edema and general reactions. When these tests show that the material is free from reactions, the solution is filled aseptically into sterile 10 cc. ampul vials. Ten containers are selected from the entire lot and each is tested for sterility. If any of these ten tested containers shows growth then ten more bottles are tested. If growth appears on retesting these new ten ampul vials, the entire lot is then reprocessed.

92. Lewis, A. A., and Turner, C. W.: The Mammogenic Hormones of the Anterior Pituitary: I. The Duct Growth Factor, Research Bulletin 310, University of Missouri College of Agriculture, Agricultural Experiment Station, 1939, pp. 1-72.

93. Lewis, A. A., and Turner, C. W.: Chemical Concentration of Mammogen from Prehypophysial Tissue, Proc. Soc. Exper. Biol. & Med. **39**: 435 (Dec.) 1938.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 28, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

CHANGES IN MAKEUP OF THE JOURNAL

Beginning with the issue for Jan. 4, 1941, the first, third and fourth cover pages of THE JOURNAL will be printed in two colors, utilizing the two color presses just installed. The change is not a radical one, involving only the use of the extra color in order to develop certain features. The general makeup and style of the cover of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION have prevailed for more than forty years and constitute such a well established form that any radical change in the nature of display type, streamlining or similar innovations has not been contemplated. In connection with the use of the additional color, the quality of the paper used for the cover has also been improved, and a finer quality of ink will be utilized.

Consideration was given also to the desirability of changes in the arrangement of the material in the reading pages. For convenience in the handling of the large amount of material which must now be rushed into THE JOURNAL because of the timeliness of articles dealing with medical preparedness and medical organization, the sections entitled "Book Notices" and "Queries and Minor Notes" have been shifted to a place just previous to the advertising pages in the back of the book. Since much of this material is constantly on hand, it is possible to make up these pages somewhat in advance of the time when the pages dealing with more current material are prepared.

This week's issue of THE JOURNAL is the index number. Readers will find that they have received for a six months period some 2,400 pages of original contributions, editorials, news material, abstracts, answers to questions, reviews of books, medicolegal information and the reports of the various councils of the American Medical Association. THE JOURNAL is proud to say that such a quantity of material of an authoritative, timely and practical character is not made available by any other medical publication in the world, even at twice the price.

THE OPTIMUM POPULATION FOR THE UNITED STATES

The changed complexion of national life which is portended by present trends in population has been discussed frequently by THE JOURNAL.[1] All the evidence of probabilities foreshadows a more or less static population or possibly a slight decrease late in this century, with a shift in age groupings resulting in a larger percentage of the total in the older years and a smaller one of children. This prospect, though contrary to an accustomed pattern, need not give rise to alarm. If, for example, the productive age group is considered to be between the ages of 20 and 65, the percentage of the total population between these ages is sure to increase for another ten years at least and will, even in the event of a slight decrease in total population, remain amply sufficient to support the groups of the population which are dependent on account of age. The percentage in the groups dependent by reason of age may not change much: with an increase in the number of elderly dependents a decrease in the number of children who are dependents is likely to occur. From a careful consideration of the probabilities, Burch [2] concludes that serious economic problems are not likely to result from this change in proportion of "youngsters" and "oldsters" and that there is little chance of dependent old people controlling the economic and political situation. Those over the age of 65 can never hope to cast more than a quarter of the total vote of the nation, even if no changes are made to restrict their political influence—a possibility with which one must reckon.

1. Headed for the Last Census? editorial, J. A. M. A. **109:** 1638 (Nov. 13) 1937; Population—Supply and Demand, ibid. **109:** 1726 (Nov. 20) 1937; Changing Population: The Premise, ibid. **111:** 1103 (Sept 17) 1938; Changing Population: The Inferences, ibid. **111:** 1189 (Sept. 24) 1938.

2. Burch, G. I.: Changing Age Composition of the American People, Population Bulletin, March 1940, Population Reference Bureau, Washington, D. C.

A favorable relationship between the number of people and the natural resources is vital to a democracy, Burch [3] believes. Although the unparalleled prosperity which the United States has enjoyed in the past has been closely associated with a rapid increase in population, it should be obvious that its continuation is not dependent on a similar rapid rate of population growth and would indeed even be hindered by a too rapid growth. Recent studies of diet, of land that can be safely cultivated and of this country's capacity to produce and consume have thrown new light on the subject of optimum population for the United States. As pointed out in a study of the Brookings Institute, it would seem that a reasonable minimum aim of our national economy would be to provide the entire population with a liberal diet which would furnish adequate nutrition, a substantial margin of safety in respect to vitamins and minerals, and a satisfying variety of foods. To reach the minimum standards proposed would require an increase in the volume of production over that existing in 1929 of all kinds of consumer goods and service by something like 70 to 80 per cent. In brief, and employing optimistic assumptions which are far removed from existent fact and may not be possible of attainment, it would require a national income of some 146 billion dollars to support 128 million persons at the minimum "optimum" standard of living and assuming an even distribution. However, the population has already exceeded this number (about 132,000,000) and the national income is only about half of the suggested figure. Furthermore, it is almost certain that the population will grow by at least 20 million more by 1980 not including foreign immigration, and even this estimate postulates a decrease of about 25 per cent in the birth rate over the next forty years.

From these studies it may be concluded that the slowing of population growth now manifest is almost certainly a desirable feature in maintaining the superior economic opportunities which place this country in a relatively favorable position as compared with the crowded countries of Europe. The figures also show that there is no need to fear either a lack of available workers or a lack of potential soldiers to meet any threat. Burch [4] likewise rejects the hypothesis that a high birth rate is a measure of vitality and a low birth rate a measure of national decadence. Economic and social conditions appear to be the real controls of the birth rate and population growth. With the picture of the true meaning of population trends becoming gradually clarified, future emphasis might be placed on quality of the population rather than on quantity alone as measured by the gross number of births. It is at least certain that there will be no shortage of workers or consumers and no overwhelming proportion of dependents in this country in the immediately visible future.

3. Burch, G. I.: A Study in Optimum Population for the United States, Population Bulletin, July 1940.
4. Burch, G. I.: The Birth Rate as a Measure of National Vitality, Population Bulletin, April 1940.

TRAFFIC IN NARCOTIC DRUGS

The U. S. Bureau of Narcotics has recently reported on the traffic in opium and other dangerous drugs for the year ended Dec. 31, 1939.[1] Contained in this report is a most interesting contrast of the prevalence of addiction to narcotic drugs in 1877 [2] and at present. In 1877, according to the report, one in every 400 persons in the United States was addicted to opium or one of its derivatives, while in 1922 and 1938, subsequent to enactment of the Harrison Narcotic Act in 1914, the ratio of such addicts to population was respectively 1 in every 1,000 and 1 in every 3,000. In the state of Michigan in 1877 there were 516 narcotic addicts per hundred thousand of population but in 1938, according to a survey conducted in Michigan by the Bureau of Narcotics in that year, there were only 17 addicts per hundred thousand. Opium or morphine eaters, prevalent in 1877, were not discovered in that survey; most of the addicts used heroin which was highly adulterated. In 1877 this country, with a population of 46,000,000, imported 350,000 pounds of raw opium but during the past few years, since importation of that drug was by law restricted to amounts necessary for medicinal and scientific needs, such imports have averaged only 150,000 pounds yearly for more than 130,000,000 people. In 1877 the average per capita consumption of opium and its derivatives was 53 grains as compared with an average consumption in 1939 of only 8.4891 grains, or 550.091 mg., per capita. The consumption of opium is no longer greatly out of proportion to medical needs. Because the supplies of heroin and morphine, the derivatives of opium commonly used by addicts, are so restricted and the prices so prohibitive, contraband drugs at the time they reach the addict are usually adulterated about 95 per cent. Consequently the average addict today obtains what amounts to less than 1 grain of his drug of addiction daily. Because of the scarcity, dilution or prohibitive price of heroin and morphine, narcotic addicts frequently resort to the use of paregoric, laudanum or the various barbituric acid derivatives. Today there are fewer female than male drug addicts, the ratio being about four males to one female, while in earlier times the reverse was the case owing to the promiscuous use of opiates for the relief of diseases of the female reproductive organs.

In 1877 physicians in many instances were directly responsible for formation of the narcotic habit by patients. Physicians too frequently resorted to the use of narcotic drugs, continued medicines too long, or, which occurred more often, prescribed indiscriminately, so that the patient continued the use of the drug indefinitely. Physicians' prescriptions for narcotic drugs were commonly refilled again and again by druggists.

1. Anslinger, H. J.: Traffic in Opium and Other Dangerous Drugs for the Year Ended Dec. 31, 1939, U. S. Treasury Department, Bureau of Narcotics, U. S. Government Printing Office, Washington, 1940.
2. Sixth annual report of the Michigan State Board of Health for the fiscal year ended Sept. 30, 1878.

Today, however, the majority of narcotic addicts are of the criminal element and are unknown to physicians and druggists. The medical profession generally is now alive to its responsibilities, and physicians, with the exception of a small minority, are more alert to the dangers surrounding the use of narcotic drugs. The indiscriminate use of narcotic medicines without intelligent medical advice, to which the spread of addiction in 1877 was attributed, is no longer prevalent. Only about 5 per cent of those addicted in 1939 gave this as a reason for their addiction. The Bureau of Narcotics attributes this improved condition in part to the efforts of the American Medical Association in publishing and distributing to the medical profession a book entitled "The Indispensable Use of Narcotics"[3] and to better instruction in medical schools. No longer is there frequent dosing of infants with opiates and no longer are family medicine cabinets and nurseries stocked with patented soothing syrups, cordials, anodynes and other preparations containing opium or its derivatives. In 1877 laudanum was a favorite drug of addiction but, to the knowledge of the Bureau of Narcotics, no addict in 1939 acquired his habit originally from the taking of this drug. The creating of an addict during childhood and continuing into the adolescent stage, which was common in 1877, no longer occurs. However, opium, particularly its derivative codeine, is still, and rightly so, the most important drug used by the medical profession.

In 1877 those who had become addicted to opium or its derivatives generally gave as their excuse for acquiring the habit that they had taken their drug of addiction in the beginning to relieve some painful or incurable disease. In 1939, according to the Bureau of Narcotics, over 60 per cent of narcotic addiction was due to association with other addicts. The use of narcotics by prostitutes is still a factor in the narcotic traffic. Narcotic addiction is still formed sometimes when a drunkard resorts to drugs for sobering effects. According to the Uniform Crime Reports for 1939, issued by the Federal Bureau of Investigation of the Department of Justice, the majority of narcotic law violators are major criminals. Of such violators arrested during 1939, 64.6 per cent had previous records and arrests.

A significant problem which still persists is the prescribing or dispensing by a relatively small number of physicians, in violation of the Harrison Narcotic Act, of large quantities of narcotic drugs to addicts, not in the course of bona fide medical treatment but solely to cater to drug addicts and to satisfy their craving for their drug of addiction. During 1939 the Bureau of Narcotics reported to the licensing agencies of the several states, for disciplinary action against physicians, 77 cases of conviction for narcotic irregularities, 62 cases of addiction and 13 cases of conviction or addiction in other states, of which 3 involved unlicensed physicians. During the year, with respect to cases of conviction, the state licensing agencies revoked the physician's license in 21 cases, suspended the physician's license in 4 cases, placed the physician on probation in 15 cases, in 10 of which narcotic privileges were withdrawn, admonished the physician in 1 case, dismissed the case without disciplinary action in 13 cases, and in 5 other cases the physician died before action could be taken. With respect to cases of addiction, the following disciplinary action was taken by the state licensing agencies: revocation of licenses 4, suspension of licenses 4, probations without narcotic privileges 12, probations 10, admonitions 2, dismissed without disciplinary action 20 and in 6 cases the physician died pending action. In the cases of conviction or addiction in other states the state licensing agencies revoked the physician's license in 5 cases, suspended the practitioner's license in 1 case and placed the physician on probation without narcotic privileges in 1 case. On Dec. 31, 1938 the cases pending action before the state licensing boards were 128 cases of conviction, 123 cases of addiction and 17 cases of conviction or addiction in other states, while on Dec. 31, 1939 the cases still pending action numbered 146 cases of conviction, 124 cases of addiction and 21 cases of conviction or addiction in other states. The Bureau of Narcotics calls attention particularly to the failure of one state licensing agency to take any action whatever in 3 cases of conviction of flagrant violation of the Harrison Narcotic Act by physicians in that state which were reported to that agency for disciplinary action. In 1 of those cases the physician issued in one year 996 prescriptions for 52,100 grains of morphine, or 208,400 doses of a quarter grain each.

In the United States the abuse of marihuana (Cannabis sativa L.) consists principally in the smoking of the resinous flowering tops and crushed portions of the plant, rolled into cigarets. The Bureau of Narcotics reports that, since the enactment of the Marihuana Tax Act of 1937, considerable progress has been made toward a solution of this nationwide problem. During the year 1939 federal and state narcotic officers seized 23,289 Kg. 606 Gm. of bulk cannabis, 34 Kg. 841 Gm. of cannabis seeds, 22,567 marihuana cigarets and approximately 930,880 cannabis plants. Also 9,026 metric tons of cannabis growing on 4,542 hectares of land were eradicated. It is estimated that the total area of uneradicated cannabis growth in this country is approximately 18,211 hectares. During 1939 the Bureau of Narcotics continued its efforts to combat the marihuana smoking practice by preventive educational work, particularly regarding the evils of marihuana. The bureau believes that direct propaganda to youth is undesirable because of the danger of arousing undue curiosity, but that it is desirable for parents, without overemphasis, to educate the youth against the use of marihuana.

3. The Indispensable Use of Narcotics, by Various Authors, Chicago, American Medical Association, 1931.

THE JOURNAL commends the enlightened and effective administration of the Bureau of Narcotics. A record such as that here reported indicates effective control. The cooperation of the medical profession has been freely and fully rendered, owing no doubt to recognition by the medical profession of the desire of the bureau to destroy criminal practice without undue interference with the legitimate prescription of narcotic drugs. Complete cooperation with the bureau by state licensing agencies will do much to further this significant work.

Current Comment

PLASMA IN TREATMENT OF ACUTE HEMORRHAGE

The present World War has enormously stimulated studies on effective substitutes for blood transfusion in treatment of hemorrhage. Recently Buttle and his co-workers [1] from the Department of Physiology, Middlesex Hospital, reported an evaluation of various blood substitutes based on controlled experiments in animals. As a result of their work they placed the substitutes in the following order of therapeutic value: (1) plasma, (2) serum, (3) hemoglobin-Ringer, (4) "gum-saline," (5) red cells suspended in "crystalloid" solution, and (6) physiologic solution of sodium chloride or isotonic dextrose solution. By way of practical accord with these conclusions, Aylward and his colleagues [2] working in Manchester report careful laboratory investigations on the technic of the concentration and drying of plasma. The dried product has several important advantages: stability, economy of storage place, ease of transport, and facility in the preparation of concentrated plasma—the latter arising from the recent recognition that there may be advantages in the use of concentrated plasma which can be readily obtained by dissolving the plasma powder in sterile distilled water to give the required concentration. Any method of drying plasma must fulfil certain conditions, the Manchester investigators point out, namely temperature control, solubility and sterility. Two principal methods of drying are available: the concentration and drying by spray distillation in vacuo, using various types of apparatus, and the concentration and drying of plasma by the cellophane tube method under sterile conditions followed by low temperature drying of the concentrate. Both these methods, they say, enable large amounts of plasma to be concentrated and dried without undue cost. These methods can be applied also to serum. The Manchester workers point out that, while the clinical effects of serum and plasma transfusions are probably similar, there are certain advantages in collecting serum rather than plasma, since serum will dry somewhat more easily than plasma owing to the absence of fibrin, sodium citrate, sodium chloride and possibly dextrose. Additional refinements of technic in the development of satisfactory and inexpensive methods of preparing blood substitutes are likely to result from the extensive studies now being made in many places.

1. Buttle, G. A. H.; Kekwick, Alan, and Schweitzer, A.: Blood Substitutes in Treatment of Acute Hemorrhage, Lancet **2**: 507 (Oct. 26) 1940.
2. Aylward, F. X.; Mainwaring, B. R. S., and Wilkinson, J. F.: The Concentration and Drying of Plasma, Brit. M. J. **2**: 4165 (Nov. 2) 1940.

EFFECT OF CHILDREN ON ECONOMIC STATUS OF AMERICAN FAMILIES

Many factors appear to be involved in the declining birth rate which has been apparent in Western countries for several decades. Lorimer [1] has recently reviewed the economic effect on American families of the appearance of children in various numbers. The most striking change in proportional expenditures in passing from families without children to families with one or more children is in the food item. At given income levels the proportions of the total family expenditures allotted to food rise consistently as the number of children in the family increases. This increased expenditure for food obviously must be offset by curtailment of other expenses. The reduction, however, is not constantly evidenced for any particular group of expenditures but appears at various points, notably household operation, furnishings and equipment, and transportation. In spite of the increased outgo for food, the average food consumption level is actually lowered as the number of children increases. Lorimer points out that if all family types invested an identical proportion of their total income in food, families with three or four children in some areas (Chicago cited specifically) would need just about twice the income of childless families in order to maintain the same consumption levels. Even farm families of several children would need more than 50 per cent larger incomes than childless families of like location. Moreover, the added expenditures for children's clothing are largely offset by reduction in the expenditure of husband and wife for their own clothing. The increased housing needs brought about by children usually result in the acceptance of more crowded quarters or moving to less satisfactory locations. The relation of total expenditure to income, i. e. the margin of savings or liability to debt, also reflects the number of children in a family. The degree of the economic effect of children varies with the income level and it influences and is influenced by the gainful employment of both parents. Indeed the entire economic outlook and practice are fundamentally involved by the addition of children to the family. Intelligent population policy requires that attention be given to these conditions. Lorimer believes it essential that some aid and support to families be established so that parents need not as at present jeopardize the standards of living which they set for themselves and their children if they wish to add new lives to the family. There are two possible approaches to equalization of levels of living among families with none or few children and large families: the family allowance proportionate to the number of children and the system of special service and subsidy to families with children along the lines developed in Sweden. In the problems which these facts present, policies concerned with population are paramount and require further research, experimentation and public attention.

1. Lorimer, Frank: The Effect of Children on the Economic Status of American Families, J. Heredity **31**: 300 (June) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

COMMITTEE ON AVIATION MEDICINE INSPECTS FACILITIES

Members of the committee on aviation medicine of the National Research Council recently made a tour of aviation medical facilities of the United States, Canada and Cuba. The group included Drs. Eugene F. Du Bois, New York, chairman of the committee; Cecil K. Drinker, Boston; John F. Fulton, New Haven, Conn.; Eugene M. Landis, Charlottesville, Va. They were accompanied by Comdr. J. F. Poppen of the U. S. Navy and Capt. Lloyd Griffis, U. S. Army. The facilities visited included Wright Field, Dayton, Ohio; the Naval Base at San Diego, Calif.; Guantanamo, Cuba, and the University of Toronto in Canada.

CIVILIANS AND HOSTILE AIRCRAFT

Dr. Gustave E. Ledfors, captain, Medical Corps, the Army Industrial College, Washington, D. C., gave a public lecture in Rochester, N. Y., December 1, under the sponsorship of the Rochester Academy of Medicine, the Medical Society of the County of Monroe and the University of Rochester School of Medicine. His subject was "Care of the Civilian Population Necessitated by Hostile Aircraft."

SARANAC LAKE MEDICAL SOCIETY

The Saranac Medical Society, Saranac Lake, N. Y., at a meeting in the Saranac Laboratory, November 13, adopted a resolution recommending that all men entering the army services receive a roentgen examination of the chest before induction into the service. The guest speakers at this meeting were Drs. S. F. Marshall and E. D. Kiefer of the Lahey Clinic, Boston, and their subject was "Medical-Surgical Treatment of Peptic Ulcer."

FIVE NEW BRIGADIER GENERALS

Five colonels of the U. S. Army Medical Department have been promoted to temporary Brigadier Generals as of October 1, according to the *Military Surgeon*. They are Brig. Gen. Albert G. Love, who will remain on duty as chief of the planning and training division in the Surgeon General's Office; Wallace DeWitt, now at Letterman General Hospital, Presidio of San Francisco; William L. Sheep, who is to be commanding general of the new army general hospital to be established in the vicinity of Atlanta, Ga.; Morrison C. Stayer, chief medical officer of the Panama Canal, and Howard McC. Snyder, who has been detailed in the Inspector General's Department.

FIELD HOSPITAL SENT TO ENGLAND

The American Field Hospital Corps has presented to the British War Relief Society a mobile field hospital of forty-one units, twenty-five trucks and trailers and sixteen weather-proof tents. The hospital, valued at $100,000, is equipped to accommodate 100 bed patients and a hospital staff of fifty. It is completely self contained and can be operated in devastated and isolated districts where shelter, power and other facilities for taking care of epidemics and the critically injured do not exist, according to the New York *Times*. The unit was taken to Staten Island, December 15, for shipment to England.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

The following additional medical reserve corps officers had been ordered to extended active duty with the regular army by direction of the War Department, Washington, D. C., up to December 13:

BELISLE, John Alexander, 1st Lieut., Mount Clemens, Mich.
CHASEN, William Henry, 1st Lieut., Brooklyn.
DALY, Joseph Michael, 1st Lieut., Laurel, Md.
EVANS, Charles Welton, Jr., 1st Lieut., Fastrill, Texas.
EWAN, John Radcliffe, 1st Lieut., Philadelphia.
GALIN, Jack, 1st Lieut., Jacksonville, Fla.
GILES, Robert W., 1st Lieut., Arkansas Pass, Texas.
GOODMAN, Eli, 1st Lieut., Chicago.
HAIMES, Solomon Manuel, 1st Lieut., Allentown, Pa.
LEVIN, Emanuel Jack, 1st Lieut., Philadelphia.
LOOMER, Harry Pincus, 1st Lieut., Brooklyn.
NICHOLS, Ace Elliott, 1st Lieut., Corpus Christi, Texas.
THOMASSY, George Ernest, 1st Lieut., Washington, D. C.
TOLOFF, Edward Myron, 1st Lieut., Pittsburgh.

FIRST CORPS AREA

The following additional medical reserve officers had been ordered to extended active duty with the regular army by the Commanding General, First Corps Area, up to December 6. The First Corps Area comprises the states of Maine, Vermont, New Hampshire, Rhode Island, Massachusetts and Connecticut.

ABRAMS, Herbert, Lieut., Lowell, Mass.
ALPERT, Max, Lieut., Bridgeport, Conn.
ANGELO, Peter, Lieut., Allston, Mass.
BERMAN, Bernard A., Lieut., Waterbury, Conn.
COYNE, Arthur A., Captain, Northampton, Mass.
HENDERSON, John W., Captain, Worcester, Mass.
HOWARD, James H., Lieut., Pittsfield, Mass.
JOSLIN, Allen P., Lieut., Boston.
MEISTER, Abraham J., Lieut., Lawrence, Mass.
PAGLIARO, Joseph J., Lieut., Derby, Conn.
PHILLIPS, Robert T., Captain, Portland, Maine.
ROSEN, Abraham E., Lieut., Bangor, Maine.
ROZEN, Alan A., Lieut., New Haven, Conn.
SEGEL, Arnold L., Lieut., Boston.
SIMARD, Louis Basil, 1st Lieut., Haverhill, Mass.
STEWART, Artemas J., Captain, Lowell, Mass.
THOMPSON, Bob F., Lieut., New Haven, Conn.
WESOLY, Andrew S., Lieut., New Britain, Conn.
WILLARD, Paul C., Lieut., Montpelier, Vt.
WITTIG, Joseph E., Lieut., West Warwick, R. I.

SECOND CORPS AREA

The following additional medical reserve officers had been ordered to active duty by the Commanding General, Second Corps Area, up to December 13. The Second Corps Area comprises the states of New York, New Jersey and Delaware.

ALEXANDER, Stewart F., 1st Lieut., Park Ridge, N. J.
AMDUR, Marvin L., 1st Lieut., Buffalo, 1st Military Area.
ANGELO, Martin A., 1st Lieut., Buffalo, 1st Military Area.
BABBITT, Hugh M., 1st Lieut., Plainfield, N. J., 3d Military Area.
BACKER, Max B., 1st Lieut., Brooklyn, 2d Military Area.
BARONE, Francis A., 1st Lieut., Jersey City, N. J., 3d Military Area.
BERGSTEIN, Joseph, Captain, Brooklyn, 2d Military Area.
BEYER, William, Major, Edgewater, N. J., 3d Military Area.
BLOOM, Bernard B., 1st Lieut., Brooklyn, 2d Military Area.
CHAMPLIN, Ray D., Lieut. Col., Oneonta, N. Y., 1st Military Area.
CHURCH, Sheldon, 1st Lieut., Albany, 1st Military Area.
DEIBERT, Kirk R., 1st Lieut., Woodlynne, N. J.
DeSIERVO, Thomas G., 1st Lieut., New York, 2d Military Area.
DOLTOLO, Joseph J., 1st Lieut., Poughkeepsie, N. Y.
ENGEL, Edward F., Captain, Seneca Falls, N. Y., 1st Military Area.
EUPHRAT, Edwin J., 1st Lieut., Flushing, N. Y.
FEINGOLD, Abraham, 1st Lieut., Brooklyn.
FORD, William G., 1st Lieut., Buffalo, 1st Military Area.
FRANK, Simon C., 1st Lieut., Williston, N. Y., 2d Military Area.
FRED, Leo, 1st Lieut., Brooklyn, 2d Military Area.
FREEMAN, Nathan, Captain, 1236 Pacific Street, Brooklyn.
GILLIS, Alfred G., Captain, Clayton, N. J., 3d Military Area.
GLENN, James A., Jr., 1st Lieut., North Creek, N. Y., 1st Military Area.
GOLDBERG, Irwin, 1st Lieut., New York, 2d Military Area.
GREENE, John E., 1st Lieut., Jamaica, N. Y.
HOFFMAN, Floyd W., 1st Lieut., Romulus, N. Y.
HOLLEY, Emerson, 1st Lieut., Lockport, N. Y., 1st Military Area.
HOWLAND, Reeve S., 1st Lieut., Elmira, N. Y., 1st Military Area.
KIVEN, Nathan J., 1st Lieut., Jamaica, N. Y., 2d Military Area.
MARKULIS, Emil J., 1st Lieut., Orchard Park, N. Y., 1st Military Area.
MARSHALL, Irving, 1st Lieut., Jersey City, N. J., 3d Military Area.
McGOWAN, John F., 1st Lieut., Buffalo, 1st Military Area.
MEISTER, Peter C., 1st Lieut., Buffalo, 1st Military Area.
MENDEN, Julian, Captain, New York.
MESSINA, John L., 1st Lieut., Brooklyn, 2d Military Area.
MORCHAN, Samuel, 1st Lieut., Angelica, N. Y., 1st Military Area.
NADLER, Arthur A., Captain, Plainfield, N. J., 3d Military Area.
NEDELL, Ralph S., 1st Lieut., Brooklyn.
O'TOOLE, John S., Jr., 1st Lieut., Potsdam, N. Y., 1st Military Area.
PATTI, Samuel R., 1st Lieut., Dunkirk, N. Y., 1st Military Area.
RITTER, Fred L., Major, Syracuse, N. Y., 1st Military Area.
ROACH, John S., 1st Lieut., Medina, N. Y., 1st Military Area.
SABIN, Anthony G., Captain, New York, 2d Military Area.
SAYER, John W., 1st Lieut., Gouverneur, N. Y., 1st Military Area.
SCHOEDEL, Adrian C., 1st Lieut., Flushing, N. Y., 2d Military Area.
SCHWARTZ, Leon J., 1st Lieut., Greenwich, N. J.
SHAEN, Edward, 1st Lieut., Camden, N. J.
STERN, Leon B., 1st Lieut., New York, 2d Military Area.
STOLA, Augustus G., 1st Lieut., New York, 2d Military Area.
TINKER, Martin B., Jr., 1st Lieut., Ithaca, N. Y., 1st Military Area.
SMUDA, Alphonse C., 1st Lieut., Glendora, N. J.
SOMMER, George N. J., Jr., 1st Lieut., Trenton, N. J.
SULLIVAN, Norbert P., Captain, Jackson Heights, N. Y., 2d Military Area.
TEGTMEYER, Charles E., 1st Lieut., Hamilton, N. Y.
WEISS, Mortimer, 1st Lieut., Hudson Falls, N. Y., 1st Military Area.
WELGE, Carl J., 1st Lieut., Roosevelt, N. Y., 2d Military Area.

Orders Not Issued

Medical reserve officers reported in THE JOURNAL, Nov. 16, 1940, page 1727, as having been ordered to active duty but whose orders have not been issued:

CREIGHTON, James J., 1st Lieut., Buffalo.
DURHAM, James R., Jr., 1st Lieut., Wilmington, Del.
HAYMAN, Charles R., 1st Lieut., Scarsdale, N. Y.
KARPEL, Bernard, 1st Lieut., New York.
KURLAND, Harry A., 1st Lieut., New York.

FOURTH CORPS AREA

The following additional medical reserve officers had been ordered to active duty by the Commanding General, Fourth Corps Area, up to December 6. The Fourth Corps Area comprises the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana:

ANDERSON, Henry L., 1st Lieut., Sellers, Ala.
BELL, Kenneth R., Captain, Sanford, Fla.
BENTON, Wayne J., 1st Lieut., Greensboro, N. C.
BERRY, Robert L., Jr., 1st Lieut., Villa Rica, Ga.
BISHOP, Louis D., 1st Lieut., DeQuincy, La.
BOOZER, Thomas S., 1st Lieut., Talladega, Ala.
BROWN, Stephen W., 1st Lieut., Milledgeville, Ga.
CLAPP, Hubert L., 1st Lieut., Swannanca, N. C.
COGDELL, David M., 1st Lieut., Fayetteville, N. C.
CORNELL, William S., Captain, Charlotte, N. C.
DENHOLM, John S., 1st Lieut., Burlington, N. C.
DISMUKES, Jackson B., Captain, Haines City, Fla.
DOTSON, Walter S., Jr., 1st Lieut., Westmoreland, Tenn.
EDWARDS, William W., 1st Lieut., Greenville, S. C.
EVERS, Herbert R., 1st Lieut., Andalusia, Ala.
EXLEY, David W., 1st Lieut., Miami Beach, Fla.
FARMER, William A., 1st Lieut., Fayetteville, N. C.
GORDON, Joseph T., 1st Lieut., Pulaski, Tenn.
GRIFFIN, Louie H., 1st Lieut., Gibson, Ga.
GRIFFIN, Taylor W., 1st Lieut., Quincy, Fla.
HATFIELD, John R., 1st Lieut., Orlando, Fla.
HAY, Floyd B., 1st Lieut., Byrdstown, Tenn.
HAUER, Douglas F., Jr., 1st Lieut., Memphis, Tenn.
HIGHTOWER, Jesse R., 1st Lieut., Itta Bena, Miss.
JACOB, Harold J., 1st Lieut., Columbus, Miss.
KING, Lebby B., 1st Lieut., Lake City, S. C.
LUSTGARTEN, Jack G., 1st Lieut., Buxton, N. C.
LYNN, Cy K., 1st Lieut., Valdese, N. C.
McMANUS, Hugh F., 1st Lieut., Raleigh, N. C.
MARTIN, Carl T., 1st Lieut., Haleyville, Ala.
MILLER, Edward S., 1st Lieut., Murphy, N. C.
MOORE, Haywood L., 1st Lieut., Porterdale, Ga.
NUNGESTER, Garrold H., 1st Lieut., Decatur, Ala.
ODEN, Lewis H., Jr., 1st Lieut., Blackshear, Ga.
PALMER, Yates S., 1st Lieut., Valdese, N. C.
PARKER, Shepherd F., 1st Lieut., Shelby, N. C.
PATTON, Marion L., Captain, Memphis, Tenn.
PEASLEY, Elmus D., Major, Raleigh, N. C.
PENTECOST, Ben L., 1st Lieut., Memphis, Tenn.
QUILLIAN, William B., Jr., 1st Lieut., Carterville, Ga.
ROBERTSON, Carroll B., 1st Lieut., Jackson, N. C.
ROBBINS, Eric P., 1st Lieut., Brockhaven, Miss.
RUSSELL, Alexander B., 1st Lieut., Winder, Ga.
RUSSELL, Ralph E., 1st Lieut., Ocala, Fla.
RUSSELL, Ralph S., 1st Lieut., Ocala, Fla.
SCHUESSLER, George D., Captain, Columbus, Ga.
SEGERSON, Edward C., 1st Lieut., Memphis, Tenn.
SHAW, Clarence, 1st Lieut., Chattanooga, Tenn.
SMAHA, Tofey G., 1st Lieut., Griffin, Ga.
SMITH, John E., 1st Lieut., Fitzgerald, Ga.
SMITH, Virgil D., 1st Lieut., Leola, Ala.
SYKES, Charlie L., 1st Lieut., Pilot Mountain, N. C.
WACHTEL, Leo M., Jr., 1st Lieut., Jacksonville, Fla.
WEEKS, Richard B., Captain, Augusta, Ga.
WELLING, Arthur W., 1st Lieut., Newberry, S. C.
WILLIAMS, Miles W., 1st Lieut., Gamilla, Ga.
WORTHY, William S., 1st Lieut., Carrollton, Ga.
YEOMANS, James W., 1st Lieut., Barnesville, Ga.
ZIRKLE, John G., 1st Lieut., Greeneville, Tenn.

Relieved from Duty

The following officers previously reported have been relieved from duty, or the orders have been revoked:

JORDAN, William K., 1st Lieut., Milledgeville, Ga.
MUSE, William S., 1st Lieut., Knoxville, Tenn.

SEVENTH CORPS AREA

Ordered to Camp Joseph T. Robinson

The following medical reserve corps officers had been ordered to extended active duty by the Commanding General, Seventh Corps Area, up to December 13, with permanent station at Camp Joseph T. Robinson, Arkansas. The Seventh Corps Area comprises the states of North Dakota, South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri, Arkansas and Wyoming.

BROWN, James Matthews, 1st Lieut., Caledonia, Minn.
BURTON, Frank Marques, 1st Lieut., Hot Springs National Park, Ark.
CLARK, Henry Bannister, Jr., Captain, St. Paul.
DALEY, Lyle Miner, Major, Hamilton, Mo.
DEVINE, John Leo, Jr., 1st Lieut., Minot, N. D.
DUNLAP, Richard Leonidas, 1st Lieut., Lawrence, Kan.
HAIGLER, James Pierre, 1st Lieut., Pittsburg, Kan.
HARRISON, Glenn Ellwood, Captain, Mason City, Iowa.
HENDERSON, Robert Wesley, Captain, Bismarck, N. D.
HOBBS, Russell Eugene, 1st Lieut., Wichita, Kan.
HOGAN, Paul Wilbur, Captain, Waukon, Iowa.
JOHNSTON, Charles Harlan, Captain, Des Moines, Iowa.
LENTZ, Harold Calvin, 1st Lieut., Neosho, Mo.
MASON, James Anders, 1st Lieut., International Falls, Minn.
MEYER, Alvin John, Captain, Lake City, Minn.
NEWKIRK, William Henry, Captain, Berryville, Ark.
PATTERSON, Harold Loyd, 1st Lieut., Lyons, Kan.
RIEGELMAN, Ralph Harold, 1st Lieut., Des Moines, Iowa.
SCHERLING, Sidney Saul, Captain, Taylors Falls, Minn.
SIEBERT, Norman Clifford, 1st Lieut., Canada, Kan.
STEINLE, George Henry, Captain, Burlington, Iowa.
STERNHILL, Irving, Captain, Mason City, Iowa.
TONEY, William Egbert, 1st Lieut., St. Joseph, Mo.
WEBSTER, LuVerne John, 1st Lieut., Battle Lake, Minn.
WILSON, William Errol, 1st Lieut., Greensburg, Kan.

The following officers are ordered to extended active duty for a period of one year with permanent station at Fort Snelling, Minnesota:

JOHNSON, Christian G., 1st Lieut., Rugby, N. D.
McCANN, Eugene John, Captain, Minneapolis.

The following officer is ordered to extended active duty for a period of one year with permanent station at Jefferson Barracks, Missouri, by the Commanding General, Seventh Corps Area:

SCHUCK, Carl Alfred, Captain, St. Louis.

The following officer is ordered to extended active duty for a period of one year with permanent station at Fort Meade, South Dakota:

NYQUIST, Roy Henning, Captain, Iroquois, S. D.

EIGHTH CORPS AREA

The following additional medical reserve officers had been ordered to active duty by the Commanding General, Eighth Corps Area, up to December 13. The Eighth Corps Area comprises the states of Colorado, Arizona, New Mexico, Oklahoma and Texas.

AARNI, John C., 1st Lieut., Hayden, Ariz.
BAGGETT, Seldon O., 1st Lieut., Austin, Texas.
BALDRIDGE, Max, 1st Lieut., Bowie, Texas.
BUKOWSKI, Lucian M., Captain, Houston, Texas.
BURNETT, Berry H., Lieut. Col., Englewood, Colo.
CANTRELL, William B., Lieut. Col., Gallup, N. M.
COCHRAN, Joel L., Major, San Antonio, Texas.
COHEN, Mayer, 1st Lieut., Marlin, Texas.
COOLEY, Ben H., Major, Norman, Okla.
DARNELL, Elmer E., Major, Colony, Okla.
DAVIS, Charles Q., Major, Houston, Texas.
DAVIS, James H., Lieut. Col., Fort Worth, Texas.
FULMER, H. Ray, 1st Lieut., Ringling, Okla.
GALLAHER, Frank C., 1st Lieut., Shawnee, Okla.
GEE, Kenneth J., 1st Lieut., Tulia, Texas.
GWINN, Frank W., Captain, Yuma, Ariz.
HARRELL, Fred S., Captain, Olney, Texas.
HAWKINS, Winfred W., Captain, Waco, Texas.
HOLTZ, Harvey E., 1st Lieut., Dallas, Texas.
JOHNSON, George H., Major, Ardmore, Okla.
KEATING, Peter M., Lieut. Col., San Antonio, Texas.
KINDER, Thurman A., Major, Brownsville, Texas.
LAPAN, Charles H., 1st Lieut., Lamar, Colo.
LEHMANN, Cornelius F., Major, San Antonio, Texas.
LITTELL, George S., Major, Dallas, Texas.
LOWIN, Julian R., 1st Lieut., Redvale, Colo.
LUBBEN, John F., Jr., Major, Dallas, Texas.
MAGID, Morston A., 1st Lieut., Denver.
MILES, John B., Captain, Anadarko, Okla.
MOORE, Isham Seller, 1st Lieut., Ozono, Texas.
MOORE, John D., Major, Fort Worth, Texas.
MURRAY, Edward Cotter, Captain, Ada, Okla.
NICHOLSON, John R., Major, San Antonio, Texas.
OLIVER, Claudius H., Lieut. Col., Douglas, Ariz.
PACE, Bedford F., 1st Lieut., Noderland, Texas.
POLLACK, Simon, 1st Lieut., Tulsa, Okla.
PRIDAY, Codric, Major, Corpus Christi, Texas.
PROSSER, Moorman P., 1st Lieut., Norman, Okla.
RAGAN, Tillman A., 1st Lieut., Fairfax, Okla.
ROBERTS, Charles J., 1st Lieut., Enid, Okla.
SAKS, Harry S., Captain, Denver.
SANFORD, Herbert M., 1st Lieut., Perryton, Texas.
SHAW, Dwight B., Captain, Pueblo, Colo.
SHORBE, Howard B., 1st Lieut., Oklahoma City.
SLAY, Iris J., Major, Fostoria, Texas.
STUARD, Charles G., Jr., 1st Lieut., Tulsa, Okla.
WALKER, Marcellus A., Jr., Captain, Paris, Texas.
WINTER, John W., Captain, San Antonio, Texas.
WOLF, Edward T., Major, Houston, Texas.

Orders Revoked

KERNEK, Paul, 1st Lieut., Oklahoma City.
TURNBOW, William Ray, 1st Lieut., Tulsa, Okla.

NAVAL RESERVE OFFICERS ORDERED TO ACTIVE DUTY

The following additional naval medical reserve officers have been ordered to active duty:

BARNES, Mark H., Lieut., M. C.-V. (S.), New York, Submarine Base, New London, Conn.
EHRLICH, Harry, Lieut. (j. g.) M. C.-V. (G.), U. S. N. R., Dispensary, Navy Yard, Brooklyn.
HARRISON, Edward K., Lieut., M. C.-V. (S.), U. S. N. R., Ossining, N. Y., Ossining Hospital, Marine Barracks, Quantico, Va.
HELD, Albert H., Lieut., M. C.-V. (G.), Huntingburg, Ind., Norfolk Naval Hospital, Portsmouth, Va.
HIGGINS, Homer A., Comdr., M. C.-V. (S.), Little Rock, Ark., to Director of Selective Service, Arkansas (Duty as State Medical Adviser).
HOEY, Waldo O., Lieut., M. C.-V. (S.), Providence, R. I., Naval Training Station, Newport, R. I.
HORST, John V., Lieut., M. C.-V. (S.), Upper Arlington, Ohio, Naval Hospital, Great Lakes, Ill.
HOYLE, Christian K. C., Lieut., M. C.-V. (S.), Roanoke, Va., Jefferson Hospital, First Marine Brigade, Fleet Marine Force, Quantico, Va.
KEIGWIN, Charles G., Lieut. (j. g.) M. C.-V. (S.), Evanston, Ill., Naval Reserve Aviation Base, Chicago.
KING, W. Ivan, Lieut. Comdr., M. C.-V. (S.), Dallas, Texas, Hospital, San Diego, Calif.
LETCHER, Charles W., Lieut., M. C.-V. (S.), Wilkes Barre, Pa., Naval Reserve Aviation Base, Philadelphia.
LEVY, Louis K., Jr., Lieut. (j. g.) M. C.-V. (S.), New Orleans, Marine Recruiting Station, New Orleans.
MARCLEY, David M., Lieut., M. C.-V. (S.), Amarillo, Texas, Naval Air Station, Jacksonville, Fla.
MILLER, Wade Hampton, Lieut. Comdr., M. C.-V. (G.), Kansas City, Mo., Naval Reserve Aviation Base, Kansas City, Kan.
MORRISON, Arlo A., Lieut., M. C.-V. (S.), Santa Barbara, Calif., Naval Hospital, San Diego, Calif.
OARD, Harry Clifford, Lieut. Comdr., M. C.-V. (S.), Jamaica, N. Y., Norfolk Naval Hospital, Portsmouth, Va.
SIMPSON, George W., Jr., Lieut., M. C.-V. (S.), Norfolk, Va., Navy Yard Dispensary, Norfolk Navy Yard, Portsmouth, Va.
WALVOORD, James H., Lieut. Comdr., M. C.-V. (S.), Hollis, N. Y., Norfolk Naval Hospital, Portsmouth, Va.
WRIGHT, Orville M., Lieut. (j. g.) M. C.-V. (G.), Nashville, Tenn., Vanderbilt University Hospital, Navy Recruiting Station, Nashville, Tenn.

AVIATION MEDICAL EXAMINERS

The following medical officers of the U. S. Army, who have been under instruction at the School of Aviation Medicine, Randolph Field, Texas, graduated as Aviation Medical Examiners, October 19:

ANDERSON, John L., Captain, M. Res., Barksdale Field, La.
BARRETT, Robert S., 1st Lieut., M. C. R., Langley Field, Va.
BILOTTA, Laurence A., Captain, M. C., Army Medical Center, Washington, D. C.
BLOUNT, Robert H., Captain, M. C., Vancouver Barracks, Wash.
BROOKS, Robert H., M. C. R., Kelly Field, Texas.
CALAWAY, William, Captain, M. C., Army Medical Center, Washington, D. C.
CAMERON, Richard R., Captain, M. C., Army Medical Center, Washington, D. C.
CROUCH, Thomas H., 1st Lieut., M. C., Fort Bliss, Texas.
DIAMOND, Max M., M. C. R., Kelly Field, Texas.
GARCIA, Charles Todd, 1st Lieut., M. C. R., Puerto Rican Department.
HARGAN, William S., Captain, M. C., Fort Benning, Ga.
JENKINS, Raymond T., Captain, M. C., Fort Bragg, N. C.
JOHNSON, Hensley S., Captain, M. C., AC Advanced Flying School, San Angelo, Texas.
KELLY, Frederick C., Captain, M. C., AC Advanced Flying School, San Angelo, Texas.
LELICH, Bronko P., 1st Lieut., M. C., Army Medical Center, Washington, D. C.
LLOYD, Harvey L., Captain, M. C., Army Medical Center, Washington, D. C.
MARKS, Maurice Isaac, 1st Lieut., M. C. R.; Maxwell Field, Ala.
MATTHEWS, John L., Captain, M. C., Texas National Guard, San Antonio, Texas.
McDONOUGH, Joseph F., 1st Lieut., M. C. R., Moffett Field, Calif.
McGREW, George D., Captain, M. C., AC Basic Flying School, Montgomery, Ala.
MORRIS, Charles K., Captain, M. C., Westover Field, Chicopee Falls, Mass.
PERRI, Frank A., 1st Lieut., Langley, Field, Va.
PIGFORD, Charles Alfred, Captain, M. Res., Maxwell Field, Ala.
SHAFFER, Frank J. 1st Lieut., M. C., AC Troops, Savannah, Ga.
SOLTZ, Gustav D., 1st Lieut., M. C. R., Lowry Field, Denver.
STAFFORD, Charles A., 1st Lieut., M. C., Fort Douglas, Utah.
TALBOT, John M., Captain, M. C., Hamilton Field, Calif.
TOWNER, Alonzo A., Jr., Captain, M. C., Fort George Wright, Wash.
WAINER, Amos S., 1st Lieut., Randolph Field, Texas.

ORGANIZATION SECTION

OFFICIAL NOTES

THE CLEVELAND SESSION

Special Exhibits on Fractures and on Lame Backs

The Committee on Scientific Exhibit announces that there will be two special exhibits at the Cleveland session as follows:

Special Exhibit on Fractures.—Presented by a committee composed of Dr. Kellogg Speed, Chicago, chairman; Dr. Frank D. Dickson, Kansas City, Mo., and Dr. Walter Estell Lee, Philadelphia.

Special Exhibit on Lame Backs.—Presented under the auspices of a committee composed of Dr. Frank R. Ober, Boston, chairman; Dr. Carl E. Badgley, Ann Arbor, Mich.; Dr. J. Archer O'Reilly, St. Louis; Dr. Arthur Steindler, Iowa City, and Dr. Philip D. Wilson, New York.

Applications for space for other exhibits close on Jan. 20, 1941. Blanks may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the A. M. A. meeting at Cleveland on June 4, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations, and no revenue is derived from the programs. Therefore, local stations may or may not take the programs, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and broadcast it at another hour or even on another day. It is advisable, therefore, to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in THE JOURNAL and monthly in *Hygeia*, The Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

January 1.* Otorhinolaryngologist.
January 8. Your Eyes.
January 12. Best Foot Forward.

* This program only will be broadcast one hour and a half earlier than the regular scheduled time in order to clear the network for international broadcasts later in the evening.

WOMAN'S AUXILIARY

National Board Meeting

The stated meeting of the board of directors of the Woman's Auxiliary to the American Medical Association was held, November 29, in Chicago with Mrs. V. E. Holcombe, Charleston, W. Va., the president, presiding.

The four past national presidents who attended were Mrs. Samuel Clark Red, Houston, Texas; Mrs. Rogers N. Herbert, Nashville, Tenn.; Mrs. Robert E. Fitzgerald, Milwaukee, and Mrs. Charles C. Tomlinson, Omaha. Mrs. R. E. Mosiman, Seattle, president-elect, was present, as were also ten members of the executive committee, ten chairmen of standing committees, sixteen state presidents, three state presidents-elect and four regional chairmen. Mr. Frank V. Cargill and Dr. W. W. Bauer were guest speakers, answering questions on *Hygeia* and the A. M. A. radio hour series respectively. Four members of the Advisory Council, Drs. Booth, Bloss, Fenton and Sensenich and Dr. Van Etten, President of the American Medical Association, were guests at lunch. Mrs. Red, first president of the national auxiliary, was guest of honor. Twelve visiting Chicago auxiliary women were also present. The nominating committee was elected and plans were made for the convention in Cleveland, June 1-6, 1941.

Preceding the board meeting, the advisory council was host at the A. M. A. headquarters at a luncheon for the executive committee of the auxiliary. Many enjoyed the opportunity of making a tour of the American Medical Association Building.

California

The auxiliary to the Los Angeles County Medical Association gave a formal dinner-dance November 5 at the Wilshire Bowl for the benefit of the Los Angeles Physicians' Aid Association. A sum of $500 was realized from the affair, which, it is planned, will be held annually for the same purpose.

Nebraska

The auxiliary to the Lancaster County Medical Society met, Nov. 4, 1940, at the home of Mrs. Wesley Becker. Mrs. A. D. Brown, state president, was a guest and spoke briefly. Mr. M. C. Smith, executive secretary to the Nebraska State Medical Association, talked to the group on medical legislation.

The Adams County Medical Association and its woman's auxiliary met for a dinner meeting at Ingleside, Nov. 6, 1940. Judge Blackledge, the after-dinner speaker, spoke on "The Story of a Witness." The auxiliary is knitting and crocheting for the Red Cross.

The officers of the six-county medical auxiliary were entertained at a luncheon, October 9, at the Perkins Hotel in David City by Mrs. R. C. Gramlich, president. Mrs. A. D. Brown was an honor guest.

Utah

The Woman's Auxiliary to the Salt Lake County Medical Society met in October at the Newhouse Hotel to discuss "Where Go the Boats," and folk lore of all nations. The afternoon was in charge of Mrs. Walter H. Horton, who, in rhyme, introduced the speakers—Mrs. L. A. Stevenson, Mrs. Richard P. Middleton, Mrs. J. Albert Peterson and Mrs. Francis Boyer. Music featuring Indian and Chinese melodies was played by Mrs. Claude L. Shields. Preceding the regular program a pageant, "Hygeia, Goddess of Health," was given by Mrs. Alfred Clawson, Mrs. Raymond Maw and Mrs. Roland Merrill. Tea and a social hour followed the program.

A business meeting of the Utah County auxiliary was held in October at the home of Mrs. Garland Pace in Provo. Mrs. Wilford Woolf, the president, was in charge of the meeting.

The state board, with Mrs. J. R. Morrell of Ogden presiding, held its meeting in October at the Lion House in Salt Lake City. Plans for the year were outlined.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Personal.—Dr. Edward F. Ellis, Fayetteville, has given his medical library of more than 1,000 volumes to the University of Arkansas School of Medicine, Little Rock.——Dr. John L. Ruff, formerly of St. Paul, has been appointed medical director for Crawford, Franklin and Logan counties, succeeding Dr. Albert S. J. Clarke, Ozark, who plans to enter the school of public health at Harvard University, it is reported.——Dr. James M. Lemons, Pine Bluff, has given his medical library to the Jefferson County Medical Society.

CALIFORNIA

Outbreak of Influenza.—A report has been received concerning the recent epidemic of influenza in San Francisco. According to Dr. Jacob C. Geiger, city health officer, the disease appeared in mild form. The incubation period ranged from three to five days and was even as short as twenty-four hours. It is estimated that 10 per cent of the population in the city was affected.

Society News.—The Los Angeles Society of Neurology and Psychiatry and the Endocrine Study Group held a joint meeting, December 18; a symposium on the hypothalamus was presented by Drs. Cyril B. Courville, Samuel J. Glass, Frederick S. Modern and Arthur R. Timme.——The speakers before the Los Angeles Society of Ophthalmology and Otolaryngology, December 23, included Drs. Daniel E. Ziskin on "Destructive Ophthalmia Associated with Atypical Erythema Multiforme," and Warren A. Wilson, "Congenital Lenticule Fibroblastic Membranes."

CONNECTICUT

Fatality from Tularemia.—The death of a man at the Newington Hospital, East Hampton, December 14, from tularemia is said to be the first from this cause in the state, according to the New York *Times*. The man cut his finger while preparing a rabbit, which he had killed on a hunting trip November 23. Five days later he showed symptoms. He became unconscious and was taken to the hospital December 9.

Course on Industrial Medicine.—The Connecticut Clinical Congress has arranged a course on industrial medicine for physicians of the state to begin January 9 at Yale University School of Medicine, New Haven. The first subject will be "Ventilation in Industry." Other subjects to be discussed are:

January 16, Pulmonary Diseases Due to Dust.
January 23, Infections in Industry.
January 30, Dermatitis and Carcinogenic Substances.
February 6, Poisoning by Benzol—Other Industrial Solvents.
February 13, Carbon Monoxide Poisoning and Other Irritant Gases.
February 20, Lead Poisoning.
February 27, Poisoning by Other Heavy Metals.
March 6, Caisson Disease and Diseases Due to Changes in Atmospheric Pressure.
March 13, Cardiac Diseases in Industry.
March 20, Adequate Nutrition for the Industrial Worker.
March 27, Medical and Health Services in Industry.
April 3, Preventive Industrial Medicine.
April 10, Legal Aspects of Occupational Diseases.

Dr. Louis H. Nahum, New Haven, is chairman of the program committee of the Clinical Congress of the state medical society.

DELAWARE

Society News.—Dr. George E. Bennett, Baltimore, discussed problems of knee joint surgery before the New Castle County Medical Society, November 19, in Wilmington.——A symposium on glaucoma is being presented by the section of ophthalmology and otolaryngology of the Delaware Academy of Medicine, Wilmington, in three meetings, November 19, December 17 and January 21. Included among the speakers are Drs. William O. LaMotte, Richard R. Tybout, Gerald O. Poole, Norman L. Cutler and William R. Hazzard.

DISTRICT OF COLUMBIA

Personal.—Dr. Rex E. Buxton, Boston, has been appointed director of the Washington Institute of Mental Hygiene, succeeding Dr. Paul J. Ewerhardt, resigned.——Dr. James A. Gannon has been appointed a member of the District board of education, newspapers report.

Society News.—Dr. Jesse G. M. Bullowa, New York, addressed a meeting of the medical and dental officers of the navy on duty in the District and vicinity, November 4, on "The Appropriate Therapy of the Pneumonias."——Dr. Evarts A. Graham, St. Louis, addressed the monthly meeting of Army Medical Department officers in Washington and vicinity at the Army Medical Center, November 18, on "Surgery of the Chest." Dr. Henry K. Mohler, Philadelphia, spoke, October 14, on "Use of Sulfanilamide and Its Associated Compounds."

GEORGIA

Industrial Hygiene Service.—The Georgia Department of Public Health has established an industrial hygiene service as a part of the division of preventable diseases to meet the increasing needs of advisory service to industries in the protection and promotion of the health of industrial workers. The service, consisting of medical and engineering advisory assistance, will soon be available to all types of industries.

Pediatric Meeting.—The Georgia Pediatric Society met at the Biltmore Hotel, Atlanta, December 12. The speakers included:

Dr. Lee Edward Farr, Wilmington, Del., Prognostic Value of Renal Function Tests in Nephritis: Role of Diet in the Therapy of Nephritis.
Dr. Samuel Z. Levine, New York, The Handicaps of Prematurity and How to Meet Them: Water and the Growing Organism.
Dr. Edward F. Bland, Boston, Manifestations of Rheumatic Fever in Childhood: Course of Rheumatic Heart Disease in Childhood and Adolescence.

Personal.—Dr. Joseph A. Johnson, Greensboro, resigned as head of the Greene County health unit, effective November 1, to accept a similar position at Toccoa in charge of the unit including Stephens, Habersham and Rabun counties.——Dr. James A. Thrash, health officer of Columbus and of Muscogee County, has been granted leave of absence until June 1941 to take special studies in health work at the University of North Carolina School of Medicine, Chapel Hill.——Dr. Roy L. Johnson, Douglas, has resigned as health commissioner in Coffee County to enter private practice.——Dr. Robert V. Schultz, New York, has been named director of public health education for the state department of health.

ILLINOIS

Society News.—Dr. Adolph L. Sahs, Iowa City, discussed "The Common Neuroses" before the Adams County Medical Society, November 11.——A symposium on diseases of the biliary tract was presented before the Coles-Cumberland County Medical Society in Mattoon, November 7, by Drs. Karl A. Meyer and Manuel E. Lichtenstein, Chicago.——Dr. Oscar F. Schultz, Evanston, was elected president of the Illinois Society of Pathologists at its annual meeting, December 7; Dr. Israel Davidsohn, Chicago, is the secretary.

Chicago

Society News.—Dr. George J. Garceau, Indianapolis, addressed the Chicago Orthopedic Society, December 13, on "Treatment of Scoliosis" and Dr. Fremont A. Chandler, "Aseptic Necrosis of the Head of the Femur."——The Chicago Pediatric Society was addressed, December 17, by Dr. Alwin C. Rambar, among others, on "The Opsono-Cytophagic Test in Pertussis Inoculation."

Study Group Named in Honor of Dr. Sonnenschein.—A medical history study group has been organized at the Michael Reese Hospital and named in honor of the late Dr. Robert Sonnenschein. The first meeting of the new group, December 11, was addressed by Dr. Reuben Friedman, assistant professor of dermatology and syphilology, Temple University School of Medicine, Philadelphia, whose subject was "Acarus Scabiei—The Story of a Twelve-Hundred Years' Search for the Obvious."

Mr. Bacon Retires as Superintendent of Presbyterian Hospital.—After more than forty years' service at Presbyterian Hospital, Asa S. Bacon will retire as superintendent, January 1. He will be succeeded by J. Dewey Lutes, who has been superintendent of Ravenswood Hospital for the last nine and one-half years. Mr. Bacon is a trustee of the American Hospital Association and has been its treasurer for thirty-five years, with the exception of one year when he served as president. In recognition of his long service, the association last February named its reference library at 18 East Division Street the Asa S. Bacon Library.

INDIANA

Personal.——Dr. George R. Douglas, Valparaiso, has been appointed health officer of Porter County, filling the vacancy caused by the death of Dr. Herman O. Seipel.

District Meeting.—Dr. Harry A. Towsley, Ann Arbor, Mich., recently addressed the Seventh District Medical Society in Franklin on "Diagnosis and Treatment of Acute Contagious Diseases." He also showed a colored motion picture on the acute stages of exanthemas.

Society News.—A symposium on arthritis was conducted before the Madison County Medical Society, November 18, in Anderson by Drs. Francis M. Williams, Frederick B. Wishard, Aubrey W. Elsten and Paul T. Lamey. All are from Anderson. —— Dr. Norman E. Freeman, Philadelphia, discussed "Peripheral Circulatory Failure: Its Prevention and Treatment" before the Indianapolis Medical Society November 26. ——Dr. Thomas M. Conley, Kokomo, discussed "Brain Tumors in Children" before the Howard County Medical Society in Kokomo, November 1.

LOUISIANA

Carville Patients Honor Perry Burgess.—The Patients' Federation and the American Legion Post of Carville, comprised entirely of leper patients, gave a reception in honor of Mr. Perry Burgess, president of the Leonard Wood Memorial, New York, and author of the book "Who Walk Alone," at the Marine Hospital, Carville, November 27. The welcome to Mr. Burgess was for the work he has been doing in behalf of leper patients. "Who Walk Alone" is the story of an American soldier who served in the Spanish-American War in the Philippines, and who became a leper many years after he had returned home.

MAINE

Society News.—Dr. Eugene E. O'Donnell discussed problems of intestinal surgery before the Portland Medical Club recently.——The York County Medical Association was addressed in Biddeford, October 9, by Dr. William J. Brickley, Boston, medical examiner for Suffolk County, on "Cause and Manner of the *Squalus* Deaths."

MARYLAND

Regulations for Occupational Diseases.—At a meeting, October 14, the Maryland State Board of Health adopted regulations for the control and prevention of occupational diseases, effective January 1. The Baltimore City Department of Health and the division of industrial hygiene of the United States Public Health Service cooperated in the formulation of the regulations. Regulation 1 is as follows:

No persons, firm, corporation or other employer shall use or permit to be used in the conduct of his business, manufacturing establishment or other place of employment, any process, material or method of working known to have an adverse effect on health, unless arrangements have been made to maintain the occupational environment in such a manner that injury to health shall not result.

Regulation 2 pertains to concentration limits and reads:

Exposures to dusts, fumes, mists, vapors, gases, or any materials that may affect health shall be kept below the following concentration limits:

Material	Concentration
Benzene (Benzol)	75 parts per million
Carbon tetrachloride	100 parts per million
Carbon monoxide	100 parts per million
Chlorine	1 part per million
Chromic acid	0.1 mg. per cubic meter

MASSACHUSETTS

Society News.—The New England Pathological Society was addressed, November 21, by Dr. Harry S. N. Greene, Princeton, N. J., on "Development of Autonomy in Spontaneous Rabbit Tumors."—— Dr. Otto J. Hermann, Boston, discussed "Convalescent Care of Fractures" before the New England Society of Physical Medicine, November 21, in Boston.—— The Essex South District Medical Society was addressed, December 4, by Dr. Walter Bauer, Boston, on "Diagnosis and Treatment of the Commoner Arthritides." Dr. James C. White, Boston, will address the society in Hathorne, January 8, on "Visceral Pain and Its Relief."—— Dr. Thomas M. Rivers, New York, delivered a Robert Dawson Evans Memorial Lecture in the Evans Memorial Auditorium, Massachusetts Memorial Hospitals, Boston, November 19, on "Elementary Bodies of Vaccine."

MICHIGAN

Changes in Health Officers.—Dr. Lorin E. Kerr, Toledo, has been appointed director of the Iron County health department, succeeding Dr. Thomas E. Camper, who is on leave of absence for graduate study at the University of Michigan, it is reported.——Dr. Buell H. Van Leuven, Petoskey, has been named health officer of Menominee County to succeed Dr. Clifford C. Corkill, who is studying at the Johns Hopkins University School of Hygiene and Public Health, Baltimore.

Society News.—Dr. Robert E. Lee, Chicago, discussed "Ambulatory Treatment of Varicosities and Associated Pathology" before the Muskegon County Medical Society, November 15.——Dr. Winthrop Morgan Phelps, Baltimore, addressed the Calhoun County Medical Society, November 18, on "The Spastic Child" and Dr. Robert B. Malcolm, Chicago, November 12, "Surgical-Pathological Conditions of the Neck."—— Dr. Richard H. Freyberg, Ann Arbor, addressed the Washtenaw County Medical Society, Ann Arbor, November 12, on "Treatment of Chronic Arthritis."——The medical section of the Wayne County Medical Society was addressed, November 11, by Dr. Joseph T. Wearn, Cleveland, on "Changes in the Coronary Circulation Resulting from Normal and Abnormal Processes."—— Among others, Dr. Frederick F. Yonkman, Detroit, addressed the Detroit Physiological Society, November 14, on "Depression of the Sympathetic Nervous System."

Annual Clinic of Highland Park Physicians' Club.—The fifteenth annual clinic of the Highland Park Physicians' Club was conducted at the Highland Park General Hospital, November 6. Included among the speakers were:

Dr. Andrew C. Ivy, Chicago, Medical Treatment of Gallbladder Disease.
Dr. Elinn F. Morse, Detroit, Pathology of Gallbladder Disease and Its Effect on the Human Body.
Dr. Willis D. Gatch, Indianapolis, Surgical Treatment of Gallbladder Disease.
Dr. Frederick A. Coller, Ann Arbor, Shock: Differential Diagnosis and Treatment.
Mr. P. A. Pranion, Detroit, Demonstration of Falling Drop Method.
Dr. Marion A. Blankenhorn, Cincinnati, Recent Advances in Vitamin Therapy.
Dr. Russell L. Haden, Cleveland, Rheumatoid Arthritis—Etiology and Treatment.
Dr. David S. Hillis, Chicago, Diagnosis of Disproportion Between Head and Pelvis.

MINNESOTA

The Bell Lecture.—Dr. Leroy U. Gardner, director, Saranac Laboratory for the Study of Tuberculosis, Saranac Lake, N. Y., delivered the seventh annual John W. Bell Lecture before the Hennepin County Medical Society, Minneapolis, December 2. His subject was "Manifestations of Tuberculosis in the Silicotic Patient."

MISSOURI

Personal.—Members of the executive faculty and the library staff of Washington University School of Medicine, St. Louis, recently observed the twenty-fifth anniversary of Miss Ella B. Lawrence as librarian. A silver bowl was presented to Miss Lawrence.——Dr. Lawrence T. Post, who recently retired as editor of the *American Journal of Ophthalmology*, was guest of honor at a dinner given by the St. Louis Ophthalmic Society at the University Club, St. Louis, November 27.

Society News.—A symposium on pneumonia was conducted before the Jackson County Medical Society, Kansas City, November 26, by Drs. John Auli, Harvey P. Boughnou and Lindsay S. Milne. All are of Kansas City.——Dr. Milton C. Winternitz, New Haven, Conn., addressed the Kansas City Academy of Medicine, November 15, on "Experimental Studies on Arteriosclerosis."——The Kansas City Society of Obstetrics and Gynecology was addressed, November 7, by Clarence W. Sondern, Ph.D., on "Newer Information on Estrogenic Substances."——Dr. Robert M. Isenberger addressed the Kansas City Urological Society, November 7, on "Pharmacology of the Urinary Antiseptics."——A symposium on infantile paralysis was presented before the Buchanan County Medical Society, St. Joseph, November 6; the speakers were Drs. William J. Hunt, Walter Roger Moore and Jacob Kulowski. All are from St. Joseph.

MONTANA

Personal.—Dr. John H. Garberson, Miles City, was recently elected governor of district 112 of the Rotary International.

Another Medical Supplement.—An eight page Health Section was published on October 13 by the *Sunday Democrat-News*, Lewiston, in cooperation with the Fergus County Medical Society.

NEBRASKA

Society News.—Dr. Newell C. Gilbert, Chicago, addressed the Omaha-Douglas County Medical Society, Omaha, November 12, on "Reflex Variations in Coronary Blood Flow." Dr. Claude F. Dixon, Rochester, Minn., was the speaker December 10 on "Surgical Diseases of the Colon."——The Five County and Madison Six County medical societies held a joint meeting in Norfolk, November 19. A symposium on fractures was presented by Drs. Robert D. Schrock and James W. Martin, Omaha, and George A. Haslam, Fremont.

NEW YORK

Institute on Radiology at Syracuse.—An institute on radiology will be held at the Syracuse University College of Medicine, Syracuse, January 18, under the sponsorship of the Central New York Roentgen Ray Society, the Medical Society of the State of New York, the division of cancer control of the New York State Department of Health and the medical college. Speakers in the afternoon will be:

Edith H. Quimby, associate physicist, Memorial Hospital, New York, Physics of Radiation for the Radiologist.
Dr. Merrill C. Sosman, Boston, Roentgenologic Aspects of Brain Tumors, Diagnosis and Treatment.
Dr. Ursus V. Portmann, Cleveland, Indications and Results of Roentgen Therapy.
Dr. Fred W. Stewart, New York, Radiosensitivity of Tumors.
Dr. Stafford L. Warren, Rochester, The Cyclotron.

At a dinner meeting Dr. Roscoe R. Spencer, assistant chief of the National Cancer Institute, U. S. Public Health Service, Bethesda, Md., will be the speaker.

New York City

Lecture on Digitalis.—Dr. Harry Gold, assistant professor of pharmacology, Cornell University Medical College, will deliver a lecture at New York Medical College, January 17, under the auspices of the Omicron chapter of Phi Delta Epsilon. Dr. Gold's subject will be "Some Recent Studies on Digitalis."

Photographic Contest for Social Hygiene Program.—The Society for the Study of Syphilis, in cooperation with the Metropolitan Camera Club Council and the U. S. Public Health Service, is sponsoring a competition for photographs to be used in public health education in venereal disease control. Merchandise prizes will be awarded for the ten best entries. For rules, the society may be addressed at Room 329, 125 Worth Street.

Personal.—Dr. Jack Masur, assistant director of Montefiore Hospital, has been appointed director of Lebanon Hospital. He will assume the position January 1, succeeding Mr. George E. Halpern, who is retiring after twenty-three years of service. Dr. Edwin L. Demuth will succeed Dr. Masur at Montefiore Hospital.——Dr. Charles F. W. Bove, for many years on the staff of the American Hospital of Paris, recently joined the staff of Gotham Hospital. Dr. Bove, a native of New York, went to France during World War I.

Dr. Humpstone Honored.—Dr. O. Paul Humpstone, chief of the department of obstetrics and gynecology at the Methodist Hospital, Brooklyn, was honored at a dinner marking his retirement from that position, December 6. Dr. Humpstone, a graduate of Columbia University College of Physicians and Surgeons in 1899, served his internship at the Methodist Hospital and has been associated with the hospital ever since. He is also professor of clinical obstetrics and gynecology at Long Island College of Medicine. At the dinner Bishop Francis J. McConnell of the Methodist Church paid tribute to Dr. Humpstone and Ralph Emerson Davis, pastor of St. Mark's Methodist Church and a member of the hospital's board of managers, presented to the guest of honor a leather-bound testimonial which bestowed on him the title of director emeritus of the division of obstetrics and gynecology.

NORTH CAROLINA

Portrait of Dr. Manning.—The alumni association of the University of North Carolina School of Medicine, Chapel Hill, recently presented to the university a portrait of Dr. Isaac H. Manning, Kenan professor emeritus of physiology and former dean of the school. Dr. William Raney Stanford, Durham, a former student under Dr. Manning, made the presentation and President Frank P. Graham accepted for the university.

Society News.—Dr. William S. Justice, Asheville, discussed "Use and Abuse of Vitamin K" before the Buncombe County Medical Society, Asheville, November 18.—— Dr. James B. Bullitt, Chapel Hill, was elected president of the North Carolina Pathological Society at its annual meeting in Charlotte, November 19, and Dr. Coy C. Carpenter, Wake Forest, reelected secretary. Dr. Charles F. Geschickter, Baltimore, was the guest speaker on "Benign and Malignant Breast Tumors."

OHIO

Morris Memorial Lecture.——The fifth annual Roger S. Morris Memorial Lecture was presented at the University of Cincinnati College of Medicine, December 11, by Bradley M. Patten, Ph.D., professor of anatomy, University of Michigan Medical School, Ann Arbor. His subject was "Age Changes in Embryonic Heart Action as Recorded in Micro-Moving Pictures and Studied Electrocardiographically."

Physicians Elected to Legislative Bodies.—Dr. Frederick C. Smith, Marion, was reelected to Congress from the eighth Ohio district, the *Ohio State Medical Journal* reports. Drs. Henry T. Phillips, Athens, and Everett LeFever, Glouster, were reelected to the state general assembly and Drs. George G. Hunter and Forrest R. Stewart, Ironton, were elected to the state senate and house of representatives, respectively.

Veteran Physicians Honored.——Dr. Norval A. Hamilton, Franklin, was guest of honor recently at a testimonial dinner attended by physicians and other friends of the Miami Valley area to celebrate his completion of fifty years in practice. Dr. Martin H. Fischer, Cincinnati, made the principal address. Dr. Hamilton was presented with a watch.——Gold plaques were presented to three physicians who have practiced fifty years or more by the Highland County Medical Society at a meeting in Hillsboro, November 6. They were Drs. John A. Mercer, Greenfield; Thomas W. Roberds, Belfast, and J. Barrett Kleckner, Lynchburg.——Six Medina County physicians who have practiced twenty-five or more years in the county were honor guests at a meeting of the Medina County Medical Society in Medina, November 14. They were Drs. Hiram P. H. Robinson, Medina; Harry Streett and Walter H. Scudder, Litchfield; Ernest L. Crum, Lodi; Edwin J. Koontz and Robert L. Johnson, Wadsworth.

OREGON

Meeting of Specialists.—The North Pacific Society of Neurology and Psychiatry held a meeting at the University of Oregon Medical School, Portland, November 9. The morning program included the following speakers: Drs. John L. Haskins, Portland, "Statistics on Admissions, Cost and Attendant Ratio of Private and State Mental Hospitals in the Northwest"; De Witt C. Burkes, Portland, "Familial Cerebellar Degeneration," and Robert H. Southcombe, Spokane, Wash., "Pyknolepsy." In the afternoon a neurologic symposium was presented as follows: Drs. John E. Raaf, Portland, "Lindau's Disease"; Charles O. Sturdevant and Thomas D. Robertson, Portland, "Multiple Sclerosis"; Laurence Selling, Portland, "Syringomyelia," and Charles P. Larson, Tacoma, Wash., and Vinton D. Sneeden, Portland, "Amaurotic Familial Idiocy (Tay-Sachs Disease)." George Bernard Noble, Ph.D., professor of political science, Reed College, Portland, was the dinner speaker.

PENNSYLVANIA

Society News.—Drs. John Royal Moore and William Edward Chamberlain, Philadelphia, addressed the Lycoming County Medical Society, Williamsport, December 13, on "Delayed Reduction of Fractures," discussing surgical and clinical aspects and roentgenologic aspects, respectively.—— Dr. Richard J. Behan, Pittsburgh, addressed the Fayette County Medical Society, Uniontown, December 5, on "Diagnosis and Control of Cancer."——Dr. Percy S. Pelouze, Philadelphia, addressed the Delaware County Medical Society, Chester, December 12, on "Urinary Bladder in Health and Disease."——Dr. Stephen A. Forbes, State College, addressed the Centre County Medical Society, Bellefonte, December 12, on "Backache, Its Causes and Treatment."——Dr. Murray B. Ferderber, Pittsburgh, discussed "The Selection of Heat in Physical Medicine" before the Mercer County Medical Society, Farrell, December 11.——Dr. William H. Guy, Pittsburgh, addressed the Blair County Medical Society at Altoona in November on "Dermatologic Manifestations of Syphilis."

Philadelphia

Annual Gross Lecture.—Dr. Virgil H. Moon, professor of pathology, Jefferson Medical College, delivered the annual Gross Lecture of the Pathological Society of Philadelphia, December 12, on "Pathology and Vascular Dynamics of Shock."

Society News.—At a meeting of the Eastern Pennsylvania Chapter of the Society of American Bacteriologists, November 26, the speakers were Dr. Esmond R. Long and Agnes B. Vogt on "Relation of Sex to the Course of Experimental Tuberculosis in Mice"; Dr. Max B. Lurie, "Relationship of Hereditary Constitution and Immunologic Factors in Resistance to Tuberculosis"; Florence B. Seibert, Ph.D., and Mr. John T. Glenn, Glenolden, Pa., "Improvements in the Preparation of Purified Protein Derivative Tuberculin," and Dr. Joseph D. Aronson, with Dr. Robert M. Saylor and Erma I. Parr, U. S. Indian Medical Service, "Incidence of Coccidioides Immitis Infection in Some Parts of the United States."

SOUTH DAKOTA

Personal.—Dr. Alpha J. Campbell, recently of Los Angeles, has been appointed chief medical officer at the Veterans' Administration Facility, Hot Springs.

Public Health Meeting.—The annual meeting of the South Dakota Public Health Association was held in Huron, October 28, with Dr. Gaylord W. Anderson, Minneapolis, as the guest speaker. Dr. Anderson spoke on "Tuberculosis Control Through Epidemiologic Investigation" and "Role of the Part-Time Health Officer."

TENNESSEE

Regional Meeting.—The semiannual meeting of the Middle Tennessee Medical Association was held in Franklin, November 21. Among other speakers were Drs. Frank J. Runyon, Clarksville, on "The Therapy of Malaria, Especially Stressing an Improved Therapeutic Test"; Tinsley R. Harrison, Nashville, "Some Clinical Aspects of Pain in the Chest"; Roscoe C. Gaw, Gainesboro, "Upper Respiratory Tract Infections and Their Influence on the Pulmonary System," and Granderson Hearn Bradley, Nashville, "Vitamins B and K in Pediatrics."

Dr. Blalock Honored for Research.—Dr. Alfred Blalock, professor of surgery, Vanderbilt University School of Medicine, Nashville, received the research medal of the Southern Medical Association at the annual meeting in Louisville, Ky., in November. The award was made in recognition of Dr. Blalock's research on circulation of the blood in cases of shock. Dr. Blalock graduated from Johns Hopkins University School of Medicine, Baltimore, in 1922 and went to Vanderbilt for a residency in 1925, becoming assistant professor of surgery in 1927 and professor in 1937.

WISCONSIN

The Bardeen Lecture.—Dr. Ernest E. Irons, Chicago, delivered the annual Charles R. Bardeen Memorial Lecture at the University of Wisconsin Medical School, Madison, December 6, on "Aspiration Pneumonia: Pathology-Bacteriology-Symptoms." The lecture is sponsored by the Phi Chi fraternity.

In Memory of Dr. Dearholt.—An all day meeting in memory of the late Dr. Hoyt E. Dearholt, Milwaukee, for many years executive secretary of the Wisconsin Anti-Tuberculosis Association, was held at the University of Wisconsin Medical School, Madison, November 26, under the auspices of the tuberculosis association and the university. Dr. James Burns Amberson Jr., New York, the guest speaker, discussed "Diagnosis of Pulmonary Tuberculosis" and "Principles of Treatment of Tuberculosis."

Society News.—Dr. Tracy J. Putnam, New York, addressed the University of Wisconsin Medical Society, Madison, November 22, on "Physiology and Treatment of Paralysis Agitans and Athetosis."——Drs. Malcolm G. Gillespie and Edward L. Tuohy, Duluth, Minn., addressed a recent meeting of the Polk County Medical Society, Webster, on "Vitamin K in Cases of Liver Depletion With and Without Jaundice" and gout.——Drs. Robert B. Osgood, Boston, and Albert A. Mertz, Decatur, Ill., addressed the Milwaukee Society of Clinical Surgery, November 26, on "Backgrounds of Bone and Joint Surgery" and "Advance in Treatment of Fractures of the Hip" respectively.—— Dr. Everett D. Plass, Iowa City, addressed the Medical Society of Milwaukee County, Milwaukee, November 8, on "Newer Advances in the General Field of Obstetrics."

GENERAL

The Bombing of England's Hospitals.—Despite the German claim that their bombing is confined to military objectives, the fact is, the Manchester *Guardian Weekly* says, that numerous nonmilitary objectives, including hospitals, churches, world famous buildings, stores, clubs, newspaper offices and other nonmilitary objectives have been bombed. The following are some of the hospitals that have been hit:

London Hospital
Queen Mary's Hospital
St. Bath's Medical School
St. Thomas's Hospital
Charter House Clinic
Ford's Hospital
Coventry Hospital
Swiss Relief Center
Great Ormond Street Hospital
St. Dunstan's Hospital
Tunbridge Wells Hospital
Royal Hospital (Chelsea)
Royal College of Surgeons

Honored for Aid to China.—Medals of honor for distinguished service to China were presented, October 25, to eleven members of the board of directors of the American Bureau for Medical Aid to China by Dr. Fu-Ching Yen, formerly national health administrator of China. Those so honored included Drs. James B. Murphy, Farn B. Chu and George B. Wallace, New York; Homer W. Smith, Sc.D., professor of physiology, New York University; Dr. George Morris Piersol, Philadelphia, and Dr. Robert R. Hannon, Albany, N. Y. Certificates accompanying the medals bore the signature of Chiang Kai-Shek and the official seal of the Executive Yuan and paid tribute to the work of the recipients for relief of China's war sufferers.

Census of Medical Manufactures.—The U. S. Bureau of the Census has released additional figures showing in detail the production of surgical supplies and equipment, orthopedic appliances and kindred products and a separate report on rubber products for use in hospitals and by the medical profession. An earlier report appeared in THE JOURNAL, November 23, page 1817. The figures are for the year 1939.

Manufacturing establishments devoted mainly to the production of surgical supplies and equipment, orthopedic appliances and kindred products produced goods during 1939 valued at the factory at 3 per cent more than those produced during 1937.

During 1939 the 360 establishments operating in this industry turned out merchandise estimated by the producers at $79,398,442. In 1937 the 323 establishments then included valued the output for that year at $77,068,094.

The 360 factories also spent nearly $5,000,000 less for materials, supplies, fuel, purchased electric energy and contract work in 1939 than did the 323 establishments two years before: $40,296,584 in 1939 compared with $45,030,602 in 1937, a difference of 10.5 per cent. With production up and cost down, the value added by manufacture was 22.1 per cent higher in 1939 than in 1937. The value added by manufacture is the value of products after the cost of materials, supplies, fuel and the like has been subtracted. This total amounted to $39,101,858 last year, compared with $32,037,492 in 1937.

Of the $79,398,442 worth of products manufactured by the 360 factories last year, $66,108,877 represented the value of surgical supplies and equipment not elsewhere classified, and orthopedic appliances alone. The difference between the first and the last quoted figure includes $223,582 received for contract work and $13,065,983 worth of products classified in other industries. In all instances the 1939 total was higher than that for 1937, when a breakdown of the production of the 323 plants in the industry revealed that $65,328,236 represented the value of surgical supplies and equipment and orthopedic appliances made, $158,444 the value of contract work and $11,581,414 the value of secondary products.

An incomplete report on the value of surgical supplies and equipment and orthopedic appliances produced in other industries last year puts the figure at $5,571,103. In 1937 this figure, when finally computed, was $5,788,762. Complete figures on this item will not be available until the final report for 1939 is issued.

The factory value of crutches, fracture appliances, elastic hosiery, abdominal supporters, braces, arch supporters, absorbent cotton and medicated plasters made during 1939 was higher than the value of those produced in 1937, while the output of artificial limbs, stumpsocks, surgical belts, suspensories, trusses, surgical gut strings, nonmedicated adhesive plasters, bandages and surgical gauze and dressings had a higher factory value in 1937 than last year.

Though the 1939 figures on sanitary napkins were not all in at the time the preliminary report was sent to the printer, the incomplete figures disclose that it was the biggest single item turned out by the industry last year. The value of the sanitary napkins so far reported is $12,984,464. In 1937 factories reported the production of this item as $14,418,756. That year, too, it was the major item turned out by the industry.

For the first time hospital, surgical and other sterilizers have been reported separately. Last year's output of these goods was valued at $1,153,680 by the manufacturers' estimates.

All figures in the report are preliminary and in several cases incomplete. These figures are subject to revision before being published in final form. Plants that had a production of less than $5,000 last year are not included in Census of Manufactures reports.

Rubber products having a value at the factory of at least three million dollars were manufactured last year. Production of hospital sheeting was valued at $1,639,519, a substantial gain over the 1937 figure of $1,072,522. These prices cover quantities of 3,857,247 square yards in 1939, compared with 2,982,123 square yards in 1937.

Surgeons' gloves produced last year had a value of $1,099,605, numbering 851,581 dozen pairs. No separate figures were obtained for this category in 1937.

In addition, an undetermined amount of medical and surgical hard rubber products are included in the 1939 total of $7,037,325 for medical and druggists' rubber sundries other than water bottles, fountain syringes, nipples and pacifiers.

Foreign Letters

BUENOS AIRES

(From Our Regular Correspondent)

Oct. 24, 1940.

Fifth Pan American Congress for Tuberculosis

The fifth Pan American Congress for Tuberculosis, in which eleven Spanish American countries with 150 delegates participated, was held in Buenos Aires and Córdoba, October 13-17. The United States was represented by Dr. Henry C. Sweany. The Oficina Sanitaria Panamericana in Washington was represented by Dr. Henson as observer. The congress was held under the auspices of the Latin-American Union of Societies for Tuberculosis, in which Argentina, Bolivia, Brazil, Colombia, Chile, Cuba, Mexico, Paraguay, Peru, Uruguay and Venezuela hold membership. Dr. Gumersindo Sayago, professor in Córdoba, presided. Argentina was represented at the opening meeting by Dr. R. S. Castillo, acting president of the Argentine Republic. The sessions were formally opened by Dr. G. Rothe, minister of the Department of Justice and Public Instruction. Dr. G. Sayago, president of the congress, linked his remarks in his opening speech to one of the chief subjects of discussion, the indexes of tuberculization in South America. He pointed out that the reports submitted by the individual countries, members of the congress, clearly revealed the presence of a common epidemiologic problem, in that tuberculosis had spread to a great extent in a uniform way. Similar geographic, racial, economic and social problems prevailed. The environmental factors of tuberculosis in Spanish American countries differed greatly from those of other countries with an older civilization. In these, general sanitation was more advanced and tuberculization had had a wider sweep. South American countries, on the other hand, rather resembled countries in which tuberculosis appeared as a new disease. Only the large South American cities presented an epidemiology analogous to that of other countries. In spite of the declining mortality rate, tuberculosis still constituted a social problem of the greatest significance. Beds available for tuberculous patients in South America were insufficient and increased the hazards of infection in the homes. Even where conditions were most favorable there was only one bed for from three to four patients who died of the disease. No effective tuberculosis control was possible without the isolation of infected persons.

The first deliberative session was held on the second day with the "Indexes of Tuberculization in South America" as the leading subject. Alejandro A. Raimondi and Julio Palacio, members of the Argentine delegation, defined the term index as representing the percentage of persons of a certain age, collectivity, race or religion who had been tuberculized. The average index for Argentina was as follows: from 0 to 6 years 44.5 per cent, from 7 to 14 years 54.1 per cent, from 15 to 20 years 67.3 per cent and above 20 years 72.3 per cent. Female incidence preponderated until the fourteenth year. The examination of 84,854 males and females at all age levels showed that 64.8 per cent presented sensitivity. Primary infection, formerly contracted more often in childhood, now appeared more often in early adulthood, the index fluctuating in Argentina between 26 and 84.2 per cent (the latter for Buenos Aires). The index for children of school age in Buenos Aires varied from 75.53 per cent in central locations to 32 in one of the suburbs. Everywhere the incidence was much lower in rural districts. Epidemiologically, tuberculous infections in Argentina show different stages of evolution regionally. In Jujuy, in the northern part of the state, a high index of 71.9 per cent prevailed together with a high mortality rate of 23.9 per 10,000 inhabitants. In the large cities, while the index was high, the mortality rate was on the decline.

In Bolivia, the epidemiologic index for the cities is high and is related to their economic condition. Because of the great frequency of anergy, vaccination with BCG is extensively recommended. In Brazil, owing to limited funds, the index remains high in comparison with European countries, which showed a decline during the last fifteen years at the ages below 20 years. Surveys in Brazil are not complete. Chile is still in the stage of massive tuberculization. The percentage of the allergic at the age of 6 years is high and the index at age 15 is 80 per cent. In Cuba the infection index, based on about 54,000 persons examined in Havana, was as high as 74 per cent in persons regarded as normal, and the morbidity rate 4 per cent; whereas it amounted to 11.7 per cent in sections of the population in which there was contact with the tuberculous. In Peru, children between 1 month and 16 years of age living in an infected environment and with tuberculin-positive reactions gave an index of 56.9 per cent, whereas in Lima, the capital of Peru, the index for children between 6 and 16 years in an apparently normal environment amounted to 65.3 per cent. In Uruguay great interest was exhibited in creating careful case lists and in the usual tuberculin tests. Sensitivity to the Mantoux test in relation to Pirquet's test was as follows: From the sixth year on the Mantoux test added 20 per cent of allergic cases to those discovered by the Pirquet tests if the positive results of the Pirquet test did not exceed 75 per cent. The formulation of international classification standards was recommended for the purpose of describing roentgenologic observations. At present great difficulties exist for the evaluation of allergy. It was also recommended that the next Pan American Congress for Tuberculosis request its member countries to conduct a systematic examination of the whole population. This would undoubtedly lower the index. In Venezuela, tuberculosis represents one of the most serious problems of public health. The mortality rate in the cities from tuberculosis varies from 210 to 470, with an average of 321 per hundred thousand inhabitants. In certain cities the mortality ranges from 12.3 to 23.16 per cent. An active pulmonary infection rate of 1.52 per cent was found in children of school age and a 3.58 per cent rate in pregnant women. The morbidity incidence is high, especially in the first years of life. It recedes between the tenth and the nineteenth year but rises again and attains its peak at age 30. No noteworthy differences in this respect were found between white and Negro persons.

HEREDITY

The subject for the second day was Heredity and Infection. Dr. A. Cetrángolo, representing the Argentine delegation, pointed out that, since immunity was not hereditary, it was difficult to understand how heredity could possess any decisive influence in evolving a human type capable of greater resistance to tuberculosis. The tuberculosis-resistant type does not represent the transmission of specific immunity but is a selective phenomenon. If the factor of heredity were as significant as assumed, the population of Europe, which had been in contact with tuberculosis for so many centuries, would be completely immune by this time. Moreover, the mortality rate for tuberculosis would not mount with economic crises. In infections, intensive bacillary invasion in persons with low nonspecific resistance evokes great hypersensitivity and low relative immunity and induces caseous processes; on the other hand, infections with low bacillary concentration provoke processes of a weakened hypersensitivity but with high relative immunity resulting in mitigated processes and allergy without morbidity. A connection exists between heredity and infection. Both factors cooperate with other factors and either promote or repel bacillary invasion. During the evolution of an infection, either grave or mild conditions will prevail in accordance with the concentration of bacilli. Heredity has only genotypic significance and is unable to bestow a specifically greater resistance.

The sessions of the third day of the congress were held in the city of Córdoba. The faculty of medicine of Córdoba has clinical opportunities because of the many sanatoriums situated in the clinically suitable province of the same name. Dr. Sofanor Novillo Corvalán, rector of the University of Córdoba, pointed out that since the first Pan American Congress held in Córdoba in 1927 the mortality incidence for tuberculosis in the city had decreased from 28.1 per 10,000 inhabitants to 17.9 in 1935, representing a reduction of 40 per cent, attributed to the systematic control of the disease. In behalf of the committee of organization, Raimondi stressed the necessity of cooperation of all South American countries. Several of these countries had recently showed an increase of tuberculosis and thus presented new problems to be solved. Population sections, immune until then, needed to be vaccinated with BCG. The European war constitutes a cause of anxiety also for the peoples of South America, because in the years to come the same factors would make themselves felt, such as a social imbalance, impoverishment and economic difficulties of all kinds. These factors either singly or collectively could lead to the spread of tuberculosis.

EXTRAPULMONARY TUBERCULOSIS

The paper, presented by Dr. Raúl A. Vaccarezza and José B. Gómez, was based on clinical and roentgenologic examinations of 420 male and female patients with extrapulmonary tuberculosis varying in age and degree of infection. Lung modifications were found in 90.2 per cent, a detailed analysis of which was presented to the congress. Extrapulmonary tuberculosis, they concluded, does not generally behave like isolated chronic tuberculosis of other body organs but tends, simultaneously or concomitantly, to become established in the systems of other organs, including the lung. Extrapulmonary tuberculosis and pulmonary tuberculosis are not mutually exclusive or antagonistic. On the contrary, the two increasingly combine. If the etiology of a disease is obscure and at the same time hematogenic modifications of the lung are observed, tuberculosis should be suspected. Patients with extrapulmonary tuberculosis ought not to be consigned to general hospital wards but be given special wards. So-called isolated chronic tuberculosis affecting an organ is not to be regarded as a local lesion but as a general condition capable of infecting other organs.

The Brazilian delegates were of the opinion that extrapulmonary cases generally represented metastasis of pulmonary lesions which spread by way of the blood stream. The Chilean delegates were in accord with this point of view and pointed out that 61 per cent of all cases of extrapulmonary tuberculosis were associated with active pulmonary lesions, 59 per cent of which represented reinfections and 2 per cent primary infections. In from 50 to 55 per cent the pulmonary pictures accompanying extrapulmonary tuberculosis show advanced and extensive lesions. Among them the mixed type predominates (31 per cent), with the diffused miliary type next in frequency (16 per cent). The presence, type and evolution of pulmonary lesions determine the prognosis of the extrapulmonary forms. Surgical wards should be established in hospitals for tuberculous diseases, closely cooperating with specialists in the field of tuberculosis. The age level at which extrapulmonary tuberculosis appears and its evolution create problems of invalidism and social dependence that make such centers desirable. Paraguay's delegates presented an extensive statistical tabulation of extrapulmonary tuberculosis occurring in their country. Peru's delegates called attention to the fact that extrapulmonary tuberculosis had not received sufficient attention in the fight on tuberculosis. Pure extrapulmonary forms, free from active pulmonary infections, amount to 24 per cent. Isolated extrapulmonary tuberculosis has mostly a renal or osteo-articular site. If pulmonary infections and extrapulmonary lesions coexist, the latter are generally of a secondary nature, indicating the collapse of allergy. The Uruguay delegates, who had studied extrapulmonary tuberculosis only in adults, observed fifty-seven cases (6.69 per cent) of extrapulmonary infection out of 852 cases of pulmonary tuberculosis. This is in accord with general experience. They concluded from the rarity of extrapulmonary lesions and the clinical and morphologic pictures that diffusion is hematogenic. Investigations made in Venezuela confirmed these observations.

Habana was chosen as the meeting place of the next congress, to convene in 1943. Dr. Juan J. Castillo, a Cuban delegate, was named as chairman. Subjects for discussion planned are the Value of BCG Vaccination, Initial Stages of Tuberculous Infections and Systematization of the Therapy in Pulmonary Cavities.

Marriages

LIEUTENANT COMMANDER JOHN MATTHEW BACHULUS, M.C., U. S. Navy, to Mrs. Grace Adams East of Oakland, Calif., October 21.

JAMES BENJAMIN SHULER, Shenandoah, Va., to Miss Mary Catherine McCarthy of Butte, Mont., in Waikiki, Hawaii, August 31.

LOUIS WILLIAMS LADD JR., Cleveland, to Miss Barbara Schutz of San Antonio, Texas, at Mount Washington, Md., September 7.

RICHARD E. EDMONDSON, Hartford, Conn., to Miss Virginia Gholson of Clarksville, Tenn., in Nashville, Tenn., in September.

GRACE HUMPHREYS HOOD, Fort Worth, Texas, to Mr. Derwood Morton of Arlington in Dallas, September 12.

KENDRICK MCCULLOUGH, Yonkers, N. Y., to DR. MARGARET WHITTAKER LAWRENCE of New York, November 8.

RUTH F. WOLCOTT, Spirit Lake, Iowa, to Mr. Otto William Fischer of Okoboji at Clear Lake, September 29.

BEN ALLEN DREIBODT, Jacksonville, Fla., to Miss Norma Elizabeth Thomas in Augusta, Ga., October 7.

MILBURN H. QUERNA, Spokane, Wash., to Miss Patty Paxton of Springdale, in Lewiston, Idaho, October 3.

EUGENE J. MAIRE, Vail, Iowa, to Miss Betty Jane Van Ackeren of Humphrey, Neb., September 17.

BROWN MCILVAINE DOBYNS, Jacksonville, Ill., to Miss Meredith Davis of Evanston in September.

OWEN M. CARROLL, New Castle, Ky., to Elizabeth Giles Thomas at Mount Sterling in October.

SHEPARD A. BURROUGHS to Miss Eleanor Mahan Hubbard, both of Ashtabula, Ohio, in October.

EINAR A. LUNDBURG, Hartford, Conn., to Miss Dorothy A. Oldfield in Burlington, Vt., June 15.

THOMAS BRICE MITCHELL to Miss Sara Elizabeth Tyson, both of Shelby, N. C., November 3.

JACK GRAHAM WEBB, Richmond, Va., to Miss Frances Skelton at Louisville, Ky., September 21.

H. FREDERICK KEIBER to Miss Marie Julian Hollan, both of Staten Island, N. Y., August 30.

ROBERT A. COEN to Miss Margaret Kernan, both of Ingleside, Neb., at Hastings, August 28.

WILLIAM J. SCHNUTE, Ann Arbor, Mich., to Miss Doris Davis of Lansing, June 29.

WENTWORTH L. OSTEEN to Miss Kate Elaine Goodson, both of Augusta, Ga., August 3.

ROBERT H. WAHL to Miss Florence Edith Hagedorn, both of Dayton, Ohio, in October.

LAD J. KUCERA, Lonsdale, Minn., to Miss Ethel Irene Benson in Omaha, September 28.

GILBERT D. KEIL, Toledo, Ohio, to Miss Carol Hoesman of Woodville in October.

LAWRENCE E. HURT to Miss Louise Conlee, both of Lexington, Ky., October 28.

LEONARD KLEIN to Miss Evelyn Rotkowitz, both of New York, November 9.

J. SAMUEL BLAIR, Gastonia, N. C., to Miss Mary Gwynne Fewell in October.

JORGE A. TRELLES to Miss Conchita Gonzalez, both of Tampa, Fla., in October.

Deaths

Carl Lucas Alsberg, Berkeley, Calif.; Columbia University College of Physicians and Surgeons, New York, 1900; assistant in physiologic chemistry, Harvard Medical School, Boston, from 1902 to 1905 and instructor of biochemistry from 1905 to 1908; chemical biologist, bureau of plant industry, United States Department of Agriculture from 1908 to 1912, and chief, bureau of chemistry, from 1912 to 1921; director of the food research institute, Stanford University, from 1921 to 1937 and since 1937 consultant; dean of graduate studies at Stanford University from 1927 to 1933; since 1937 director of the Giannini Foundation of Agricultural Economics at the University of California; during the World War was chief chemist for the department of agriculture in the War Industries Board; member of the advisory committee on land utilization of the National Resources Planning Board; member of the American Society of Biological Chemists, of which he was a former president, American Chemical Society, for which he was a councilor and associate editor of its journal, and the Washington Academy of Sciences, of which he was a former president; aged 63; died, October 31, in the Alta Bates Hospital of pneumonia.

John Augustus Hartwell, New York; Yale University School of Medicine, New Haven, Conn., 1892; professor of clinical surgery emeritus at Cornell University Medical College, where he was for many years associate professor of surgery and professor of clinical surgery; president of the New York Academy of Medicine from 1929 to 1932 and director from 1934 to 1938; was an associate director of the American Society for the Control of Cancer; member of the Medical Society of the State of New York, the American Surgical Association and the Society of Clinical Surgery; fellow of the American College of Surgeons; served during the World War; consulting surgeon, Bellevue, Reconstruction, Presbyterian, Memorial and Lincoln hospitals, New York, Lawrence Hospital, Bronxville, and United Hospital, Port Chester; aged 71; died, November 30, in Oakdale, N. Y., of pulmonary embolism.

Henry Hurd Rusby, Sarasota, Fla.; University of the City of New York Medical Department, 1885; member of the Medical Society of New Jersey; professor of botany, physiology and materia medica, College of Pharmacy, Columbia University, New York, from 1888 to 1930 and dean from 1904 to 1930; professor of materia medica, University and Bellevue Hospital Medical College, New York, from 1897 to 1902; president of the American Pharmaceutical Association, 1909-1910; pharmacognosist in Bureau of Chemistry, United States Department of Agriculture, from 1912 to 1917; was awarded the Remington Medal of the American Pharmaceutical Association in 1923; author of numerous books; aged 85; died, November 18, of intestinal obstruction.

Joseph Nelson Davis ✠ Twin Falls, Idaho; Kansas Medical College, Medical Department of Washburn College, Topeka, 1907; served as secretary-treasurer of the Idaho State Medical Association from 1922 to 1931, when he was made president-elect, from 1935 to 1938 councilor and in 1938 again elected secretary-treasurer, serving until this year, when he asked to be relieved; served during the World War; on the staff of the Twin Falls County General Hospital; state chairman for the Committee on Medical Preparedness of the American Medical Association; aged 58; died, November 5, of injuries received in an automobile accident.

Frank Eliot West, Brooklyn; Long Island College Hospital, Brooklyn, 1876; professor of materia medica and therapeutics and clinical medicine at his alma mater from 1886 to 1921 and since 1921 emeritus professor of therapeutics and clinical medicine; member of the Medical Society of the State of New York; censor in 1878, vice president in 1890, president in 1891 and trustee from 1892 to 1902 of the Kings County Medical Society; served at various times and in various capacities on the staffs of the Kings County Hospital, Long Island College Hospital and the Brooklyn Hospital; aged 90; died, November 21.

Willard D. Duckworth, New Rochelle, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York; 1909; member of the American Roentgen Ray Society and the Radiological Society of North America; at one time assistant professor of roentgenology at the New York Post-Graduate Medical School, Columbia University; aged 57; on the staffs of the New Rochelle (N. Y.) Hospital, Tarrytown (N. Y.) Hospital, Grasslands Hospital, Valhalla, and the White Plains (N. Y.) Hospital, where he died, November 11, of cerebral hemorrhage.

Frank Newton Irwin, White Plains, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; member of the Medical Society of the State of New York; adjunct professor of ophthalmology at the New York Post Graduate Hospital and Medical School from 1902 to 1907; consulting ophthalmologist, Manhattan Eye, Ear and Throat Hospital, New York; New York Hospital-Westchester Division, White Plains Hospital, St. Agnes Hospital and Winifred Masterson Burke Relief Foundation, Sharon (Conn.) Hospital and St. John's Riverside Hospital, Yonkers; aged 75; died, November 11.

Leonard Knight Graves, Elmhurst, N. Y.; Columbian University Medical Department, Washington, D. C., 1885; Bellevue Hospital Medical College, New York, 1887; member of the Medical Society of the State of New York; veteran of the Spanish-American and World wars; formerly an inspector in the New York Health Department; for many years on the staff of the New York Eye and Ear Infirmary, New York; aged 84; died, November 12, in the Veterans Administration Facility, New York.

David Sturges Fairchild Jr. ✠ Colonel, United States Army, retired, New York; Drake University Medical Department, Des Moines, 1897; veteran of the Spanish-American and World wars; was commissioned a lieutenant colonel in the medical corps of the regular army in 1920 and in 1930 a colonel; retired in 1935 for disability in line of duty; fellow of the American College of Surgeons; aged 69; died in November at Waynesboro, Va., of injuries received in an automobile accident.

Daniel Warwick Harmon ✠ Colonel, M. C., United States Army, Hot Springs National Park, Ark.; University of Virginia Department of Medicine, Charlottesville, 1903; fellow of the American College of Surgeons; commissioned a first lieutenant in the medical corps of the army in 1909, a lieutenant colonel in 1929 and colonel in 1935; served during the World War; was commanding officer of the Army and Navy General Hospital; aged 60; died, November 8, of heart disease.

John King Freeman ✠ Louisville, Ky.; University of Louisville Medical Department, 1894; at one time adjunct professor of abdominal surgery and gynecology at his alma mater; past president of the Jefferson County Medical Society; veteran of the Spanish-American and World wars; aged 73; for many years on the staff of the SS. Mary and Elizabeth Hospital, where he died, November 6, of hypertrophy of the prostate, uremia and coronary sclerosis.

Edwin Charles Ebert ✠ Commander, United States Navy, Long Beach, Calif.; Marquette University School of Medicine, Milwaukee, 1916; was commissioned an assistant surgeon in the Medical Corps of the United States Navy in 1917, lieutenant in 1920, lieutenant commander in 1925 and commander in 1935; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; aged 50; died, November 4.

Joseph Thomas Buxton ✠ Newport News, Va.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the House of Delegates of the American Medical Association in 1920, 1922 and 1924; member of the Southern Surgical Association; fellow of the American College of Surgeons; surgeon in chief of the Elizabeth Buxton Hospital; aged 64; died, November 5, of coronary thrombosis and arteriosclerosis.

Joseph Augustus Crisler ✠ Memphis, Tenn.; Memphis Hospital Medical College, 1890; past president of the Shelby County Medical Society; member of the Southern Surgical Association and the Southern Society of Clinical Surgeons; fellow of the American College of Surgeons; aged 72; died, November 18, of cerebral hemorrhage.

Jay Harvey Bacon ✠ Peoria, Ill.; Johns Hopkins University School of Medicine, Baltimore, 1904; member of the Clinical Orthopedic Society; fellow of the American College of Surgeons; served during the World War; on the staff of the Methodist Hospital; formerly on the staff of the Proctor Hospital; aged 63; died, November 18, of arteriosclerotic heart disease.

James Andrew Brown ✠ Commander, U. S. Navy, San Diego, Calif.; Ohio State University College of Medicine, Columbus, 1917; appointed assistant surgeon in 1917, promoted to the rank of lieutenant in 1920, lieutenant commander in 1925 and commander in 1935; aged 47; died, November 16, in the United States Naval Hospital of chronic myocarditis and nephritis.

Frank Taylor Andrews, Pasadena, Calif.; Chicago Medical College, 1884; member of the Illinois State Medical Society; professor emeritus of gynecology at his alma mater, now the Northwestern University Medical School; fellow of the American College of Surgeons; aged 82; died, November 7, of arteriosclerosis.

Percy Daniel Hoover ✠ Waynesboro, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; member of the board of trustees of Gettysburg (Pa.) College, and its secretary for many years; on the staff of the Waynesboro Hospital; aged 68; died, November 14.

Joseph Warrington Crawford ✠ North Adams, Mass.; Hahnemann Medical College and Hospital of Philadelphia, 1900; member of the Radiological Society of North America; on the staff of the North Adams Hospital; aged 68; died, November 7, of coronary sclerosis.

Byron Haskin, Theresa, N. Y.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1903; member of the Medical Society of the State of New York; since 1921 health officer of the consolidated health district of Theresa; aged 68; died, November 7.

Clark Wilder Hawley ✠ Chicago; Rush Medical College, Chicago, 1885; an Affiliate Fellow of the American Medical Association; member of the American Academy of Ophthalmology and Otolaryngology; aged 85; died, November 1, in La Grange, Ill.

Frederick Lincoln Emerson ✠ Boston; Boston University School of Medicine, 1892; served in various capacities on the staff of the Massachusetts Memorial Hospitals; for many years on the staff of the Brooks Hospital, Brookline; aged 78; died, November 10.

Siegfried Jackson, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; member of the Illinois State Medical Society; on the staff of the Columbus Hospital; aged 65; died, November 6.

Nellie Calista Flint, Mount Pleasant, Iowa; Hahnemann Medical College and Hospital, Chicago, 1899; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; aged 74; died, November 3.

William Francis Cunningham ✠ New York; Yale University School of Medicine, New Haven, Conn., 1911; served during the World War; on the staff of the Roosevelt Hospital; aged 51; died, November 19, in the Doctor's Hospital.

Joel Herbert Carter, Castleberry, Ala.; University of Alabama School of Medicine, 1910; member of the Medical Association of the State of Alabama; member of the county board of education; aged 59; died in November.

Samuel Scott Blacklock ✠ Hibbing, Minn.; Rush Medical College, Chicago, 1901; fellow of the American College of Surgeons; medical superintendent of the Rood Hospital; aged 66; died, November 12, of coronary thrombosis.

John Joseph Kenney ✠ Providence, R. I.; Dartmouth Medical School, Hanover, N. H., 1908; on the staffs of St. Joseph's, Homeopathic and Lying-In hospitals; aged 56; died, November 7, in the Jane Brown Hospital.

David Wendell Eames, Kecoughtan, Va.; University of the South Medical Department, Sewanee, Tenn., 1908; on the staff of the Veterans Administration Facility; aged 54; died, November 9, of coronary occlusion.

Mary Jardine Evans, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1935; member of the Medical Society of the State of Pennsylvania; aged 44; died, November 6, of tuberculosis.

Jean Girouard, Longueuil, Que., Canada; School of Medicine and Surgery of Montreal, Que., 1879; member of the legislative council from 1899 to 1937; formerly school commissioner; aged 84; died, November 12.

Michael Scott Kearns, Fort Lauderdale, Fla.; St. Louis University School of Medicine, 1926; formerly coroner of Hamilton County, Ohio; served during the World War; aged 40; died, November 14.

Tom Morford Throckmorton, Chariton, Iowa; Jefferson Medical College of Philadelphia, 1877; member of the Iowa State Medical Society; aged 88; died, October 31, in Des Moines of myocarditis.

Thomas Wayne Hancock, Lufkin, Texas; National University of Arts and Sciences Medical Department, St. Louis, 1913; aged 59; was killed, November 4, in an automobile accident.

Robert McKay Greenshields ✠ Romeo, Mich.; Detroit College of Medicine, 1900; served during the World War; aged 67; died, November 15, in the Jennings Hospital, Detroit.

James Henry Maynard ✠ Adair, Iowa; Rush Medical College, Chicago, 1899; past president of the Cass County Medical Society; aged 67; died, October 18, of acute myocarditis.

Gustavo Testa, Waterbury, Conn.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1902; aged 61; died, October 23, of coronary sclerosis and myocarditis.

John W. Barber, Yokena, Miss.; Kentucky School of Medicine, Louisville, 1884; aged 90; died, November 2, at Edwards of chronic myocarditis, hypertrophy and arteriosclerosis.

Nat Taylor Dulaney Jr., Bristol, Tenn.; Tennessee Medical College, Knoxville, 1893; aged 70; died, November 15, in the King's Mountain Memorial Hospital, Bristol, Va.

Simon Jay Mason, New York; University of Cincinnati College of Medicine, 1936; member of the Medical Society of the State of New York; aged 31; died, November 12.

Albert George Jenner, Milwaukee; University of Pennsylvania Department of Medicine, Philadelphia, 1897; served during the World War; aged 64; died, November 10.

Frederick Hubert Ladd, Canton, N. Y.; Albany (N. Y.) Medical College, 1902; member of the Medical Society of the State of New York; died, October 19.

Taylor Boyd Dixon, Washington, D. C.; Columbian University Medical Department, Washington, 1900; aged 64; died, November 2, of coronary thrombosis.

Robert James Baird, Creston, Ohio; Western Reserve University Medical Department, Cleveland, 1885; aged 87; died, November 3, of cerebral sclerosis.

Timothy Deason, Brachfield, Texas (licensed in Texas under the Act of 1907); aged 84; died, November 5, of heart disease and hypertrophic arthritis.

Harvey Baker Powers, Saranac Lake, N. Y.; University of Pittsburgh School of Medicine, 1920; aged 45; died, October 18, of pulmonary tuberculosis.

Frank Le Count Dowe, New York; New York Homeopathic Medical College and Flower Hospital, New York, 1889; aged 73; died, November 18.

Frank Leonidas Hall, Hannibal, Mo.; Rush Medical College, Chicago, 1887; at one time member of the state legislature; aged 79; died, November 11.

William Wirt Harvey, Boston; Harvard Medical School, Boston, 1898; member of the Massachusetts Medical Society; aged 74; died, November 10.

William Marshall Hinkle, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1891; aged 77; died, November 21.

Albert A. Duclos, Wisconsin Dells, Wis.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1895; aged 79; died, November 4.

Alvin Gustav Berger ✠ Chicago; Eclectic Medical College, Cincinnati, 1916; on the staff of the Grant Hospital; aged 48; died, November 9.

Morris Fallick, New York; Eclectic Medical College of the City of New York, 1905; aged 55; died, November 13, in the Lebanon Hospital.

Samuel Lumpkin Starks, Washington, D. C.; Howard University College of Medicine, Washington, 1920; aged 60; died, October 28.

Irving Edwin Burtnette, Morrice, Mich.; Hahnemann Medical College and Hospital, Chicago, 1898; aged 72; died, November 16.

Robert Tinion Hodgson Jr., Wilkinsburg, Pa.; University of Pittsburgh School of Medicine, 1924; aged 41; died, November 6.

Robert Nelson Buckmaster, Pangburn, Ark.; Gate City Medical College, Dallas, Texas, 1907; aged 71; died, November 17.

Thomas J. Hendrick, Webster, Ky.; Kentucky School of Medicine, Louisville, 1883; aged 80; died, November 6.

Charles J. Ayres, Newbern, Ala.; Medical College of Virginia, Richmond, 1886; aged 70; died, November 12.

Claude Bell, Tuscaloosa, Ala.; Chattanooga (Tenn.) Medical College, 1904; aged 64; died, November 3.

Ernst Theodor Hein, Palouse, Wash.; Baltimore Medical College, 1888; aged 84; died, October 3.

Bureau of Investigation

TWO FRAUDULENT "DIABETES CURES"

The Post Office Department has in the past debarred some "diabetes cures" from the mails, properly taking the stand that anything sold as an immediate or gradual substitute for insulin is an obvious fraud, and particularly dangerous when recommended for self treatment of the condition.

Dr. Samuel E. Edmunds' Concern

From Charleroi and Jeannette, Pa., Samuel E. Edmunds, M.D., and N. Edmunds, described as his wife, put out a mail-order nostrum, "Diabeto." It is said that Dr. Edmunds started the enterprise in 1938, renting a postoffice box at Jeannette, Pa., and doing business under his wife's name for what he called "ethical reasons." This is a timeworn excuse given by renegade physicians who hope to escape notoriety for their quackery by keeping their identities under cover.

"N. Edmunds" advertised that a "New German Remedy" for diabetes was "giving wonderful results" and that a six weeks supply could be had for $5. Readers who responded received personal letters urging the purchase of Diabeto and advising that by the use of it "many" diabetic patients "get away" from the use of insulin. Also there was a questionnaire to be filled out, on the basis of which the customer was to receive "personal" advice on his case.

These facts were brought out in the memorandum submitted on the matter by Judge Vincent M. Miles, Post Office Solicitor. This document went on to show that persons who returned the questionnaire with the information that they had long been afflicted with sugar diabetes and were under physicians' care involving the use of a restricted diet and the injection of from 15 to 30 units of insulin daily, and who ordered Diabeto on the express basis that it be sent them *if* it would rid them of diabetes and enable them to discontinue dieting and using insulin, were furnished with Edmunds' nostrum.

Also it was shown that, instead of "personal" advice, Edmunds sent all remitters only stereotyped letters advising them to eat slowly, chew their food well, and purchase laxatives such as citrate of magnesia, Sal Hepatica, Glauber's salt and sodium phosphate. *There were also mimeographed dietary sheets that forbade the use of a wide variety of foods, although Edmunds had led customers to believe that by the use of his treatment they could return to a normal diet. Further, although before they purchased it he had claimed that it would enable them to discontinue taking insulin, after they had undertaken his treatment he advised them to continue using insulin indefinitely.*

Edmunds was quoted as saying that his product was based on a German compound, "Sepdelen," of which he claimed to have heard through an individual who allegedly had recovered from diabetic leg ulcers through the use of Sepdelen. The memorandum brought out that Diabeto was essentially a mixture of four of the sodium salts—the sulfate, tartrate, citrate and phosphate, all common saline laxatives. It also emphasized that it is necessary for a person with diabetes to follow a carefully weighed and balanced diet, with routine injection of insulin, and that there is no drug or combination of drugs known to medical science that is a satisfactory substitute for insulin. It was further pointed out that neither Diabeto nor any other drug nor combination of drugs was known to science as being capable of restoring to normal health the cells of the pancreas gland which have been damaged, atrophied or destroyed. On the contrary, it was shown that a product like Diabeto would injure the patient by keeping him in a state of constant laxation which not only would not control the amount of sugar and other toxins present in his blood but would also debilitate him because of continued loss of minerals and other nutritive substances through the bowels.

As the promoters of the scheme were unable to offer any scientific evidence to support their claims for Diabeto, the solicitor recommended that a fraud order be issued against the names under which they did business—N. Edmunds, Samuel E. Edmunds, M.D. and S. E. Edmunds, M.D. at Charleroi and Jeannette, Pa. It was issued on Dec. 13, 1939.

A Dr. S. E. Edmunds who may have been the person mentioned was listed as "Medical Counselor" on a letterhead of Lee & Company, Philadelphia, that was sent out in August 1939, accompanied by a circular showing that the Lee concern was advertising "Fru-min Salts, formerly German Fruit Salts," also described as "The New Bio-Chemical Therapy for acute, chronic, lingering diseases, treating the CAUSE, composed of 13 remedies, 39 strengths." Although the stuff, from the claims and testimonials cited, purported to be something of a cure-all, the circular declared "We specialize in diabetes." The fact that it was also represented to come from Europe indicates that it may have been identical with or similar to the Sepdelen or Diabeto that has been mentioned.

The circular in question bore the rubber stamp of H. Landgraf, Philadelphia. THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION for Oct. 27, 1934, carried an article detailing the case of a Post Office fraud order issued against H. Landgraf and his "German Fruit Salts," represented as a veritable cure-all and especially played up for diabetes. The article also brought out that Landgraf was then apparently trying to circumvent the fraud order by putting out a diabetes nostrum under the trade style of "Hilton Chemical Company" at Philadelphia.

Samuel Ernest Edmunds appears in the American Medical Association's records as a graduate of the Atlantic Medical College, Baltimore, in 1910 (the year it became defunct) and as obtaining, in the same year, licenses to practice in Pennsylvania and Maryland, the latter issued by the homeopathic board. He is not shown as a member of his local medical society.

National Diabetic Food Company

Under the foregoing title and also the name "National Diabetik Food Company" a George H. Keys and an R. Randall put out from Kansas City, Mo., "National Diabetic Food" and "National Mineral Ration." The Post Office Department's investigation revealed that these promoters had been in the "diabetes cure" game since 1936, though neither possessed any medical training or experience, nor was any one with such qualifications connected with the company.

Victims were lured by such advertising claims as:

> No matter how bad or how long you have suffered, you can now get a treatment that has relieved some of the worst cases we have seen. No drugs or complicated directions. . . .

To persons who "bit" the concern sent printed form letters containing such preposterous misrepresentations as that the causes of diabetes prevail in over two thirds of the American homes and that the remedy lies in National Diabetic Food and its accessory product, National Mineral Ration, through the use of which a person with diabetes would be able to resume a normal diet and gradually quit the use of insulin altogether.

Judge Vincent M. Miles, Solicitor for the Post Office Department, brought out in his memorandum on the case that National Diabetic Food was pulverized and prepared for sale by the promoters in their homes from a weed called saltbush, which they obtained at no cost from farms around Kansas City. Chemical and microscopic analysis in government laboratories showed that it was composed essentially of traces of calcium, iron, phosphate, sodium, potassium and chloride in the form of plant ash.

Similar analysis of National Mineral Ration, the supplementary product which the concern obtained from an Indianapolis concern, revealed that it was essentially composed of minute amounts of epsom salt, calcium, iron, manganese, sodium, potassium, ammonia, carbonate, bicarbonate, sulfate, chloride and sulfur, with traces of iodides, bromides and possibly of copper, zinc and lithium.

The solicitor's memorandum declared that these mixtures, whether used singly or in combination, were absolutely worthless for treating diabetes, a condition due to lack of insulin, a hormone normally secreted by special cells of the pancreas gland which are known as the "islands of Langerhans." The memorandum went on to show that diabetes is characterized by the faulty metabolism of sugars, fats and starches, and the presence of excess sugar, acids and other toxic bodies in the blood and urine; that diabetes is incurable but may be effectively controlled, and blood sugar kept at a normal level by constant use of a

carefully weighed and balanced diet; and that in addition to stringent dietary measures severe cases require routine injections of insulin to compensate for the body deficiency therein.

Further, evidence was presented to show that certain diabetic patients who were treated with saltbush lapsed into diabetic coma both while taking and shortly after they had ceased using it, and that the prolonged use of it had resulted in the deaths of some such patients.

An interesting sidelight on the case was brought out in the revelation that the wife of one of the promoters had died of diabetes while taking these nostrums, which fact he admitted, though he attributed her death to her failure to follow a proper diet. Another feature of the hearing was the defendants' claim that their National Mineral Ration had been analyzed and passed by the Indiana State Board of Health, whereas the Post Office presented information from that board that this claim was untrue.

The conclusion of the solicitor was that there was sufficient evidence that the business was a scheme for obtaining money illegally through the mails, and he recommended the issuance of a fraud order. This was issued on Feb. 1, 1940, against the names National Diabetic Food Co., National Diabetic Food Company, National Diabetik Food Company, Geo. H. Keys, Ps.D., R. Randall, and their officers and agents as such.

The concern, however, like many other outfits that have perpetrated swindles by mail, simply changed its name and continued to do business. In a new memorandum issued by Judge Miles on May 28, 1940, he said of this scheme, in part:

> Evidence now before me shows that George H. Keys, in an attempt to evade the effect of the fraud order against the National Diabetic Food Company enterprise, has adopted the assumed and fictitious title of Natur-Food Company, under which name form letters and mimeographed circular matter are being sent through the mails to former customers and others advising them that further purchases of "National Dibetik Food" and "National Minral Ration" may be made from the Natur-Food Company and furnishing a business reply envelope addressed to Natur-Food Company, P. O. Box 2623, Kansas City, Missouri, for that purpose. One of these form letters, on the letterhead of "Tru-Science," reads in part as follows:
>
> Dear Friend:* * *
>
> It seems that a technical error has arisen which is causing the NATIONAL DIBETIK FOOD COMPANY considerable trouble. They believe that, because of the nature of the information that is given out to the public, a large national association is behind this action.
>
> The NATUR-FOOD COMPANY IS HANDLING NATIONAL DIBETIK FOOD, NATIONAL MINRAL RATION and ELECTREAT MECHANICAL HEART. The same offers, prices and information are available. In ordering, ORDER FROM—
>
> NATUR-FOOD COMPANY
> P. O. Box 2623
> Kansas City, Mo.
>
> Save this address for future correspondence. MAKE ALL CHECKS AND MONEY ORDERS PAYABLE TO NATUR-FOOD COMPANY. Miss Velma L. Hanson is in charge of the NATUR-FOOD COMPANY and will extend you the same courteous and prompt service that has been the policy of the NATIONAL DIBETIK FOOD COMPANY to give its many customers throughout the nation. The NATUR-FOOD COMPANY will be very pleased to have you order from them.* * *
>
> The evidence further shows that the preparations "National Dibetik Food" and "National Minral Ration" have actually been sold through the mails by Natur-Food Company in response to an inquiry addressed to that concern specifying that the products were desired for use by a diabetic sufferer in place of insulin. Accompanying the preparations was a mimeographed treatise upon the history and alleged value of saltbush (National Dibetik Food) if used continuously, in the treatment of mild, severe, long-standing and gangrenous cases of diabetes. This article bears the signature of T. R. Randall, one of the promoters of the original National Diabetic Food Company enterprise. Attached to this dissertation was a series of mimeographed questions and answers on the subject of the use of saltbush. . . .
>
> The evidence before me shows, and I so find, that this is a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises and is an evasion of the fraud order of February 1, 1940.
>
> While it appears that the name "Tru-Science" is also used in certain instances in such a manner as to imply some connection with the Natur-Food Company, inasmuch as persons solicited are directed to make all checks and money orders for the products purveyed herein payable to the latter concern, it is believed that the extension of the fraud order of February 1, 1940, to cover the name Natur-Food Company only will effectively suppress this scheme.
>
> I therefore recommend that a supplemental fraud order be issued against Natur-Food Company, Natur-Food Co., and their officers and agents as such, at Kansas City, Missouri.

This order was issued on May 28, 1940.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

CARDIAC ACTIONS OF QUINIDINE AND DIGITALIS

To the Editor:—**While reading the article by Dr. Levy on cardiac arrhythmia in the Sept. 7, 1940, issue of The Journal I encountered an old problem of mine. I cannot get a consensus about the comparative actions on the myocardium, auriculoventricular conduction and so on of quinidine and digitalis. In fact, many of the standard textbooks appear to contradict one another in the application of the principles of what these drugs are said to do. The matter has caused considerable argument among my friends and I would appreciate some information on the matter.**

M.D., Tennessee.

ANSWER.—Digitalis and quinidine are both valuable remedies for patients with cardiac disease but each has its elected place in cardiac therapy. When each drug is properly used and the limits of its actions are known and its specific indications recognized, much benefit may be expected.

Quinidine, a protoplasmic poison, is known to act directly on the myocardium. It decreases its irritability. It also is known to depress auriculoventricular conduction and to prolong the rate of intraventricular conduction. Although the actual refractory period of auricular muscle may not be prolonged, as pointed out by Love, it is the opinion of Lewis and Drury that the effective refractory period is prolonged by delay of the spread of the impulse through the auricular muscle. It produces vagal depression and occasionally by slowing the rate of the fibrillating auricle it also acts to increase the ventricular rate. It is known that, in 60 per cent of cases of auricular fibrillation, quinidine has been successful in restoring normal sinus rhythm. It is apparently most successful in the cases of fibrillation of short duration or of the paroxysmal type, although it is also occasionally effective in cases of many years' duration. It is least valuable in instances of fibrillation associated with severe cardiac insufficiency and it is here that it has its greatest dangers. It is now believed that it should not be used for patients with marked cardiac disease or auricular fibrillation of many years' duration associated with cardiac enlargement, because of the possibility of producing cardiac standstill. Premature auricular systoles, occurring singly or in short runs, are usually depressed by the use of quinidine. Ventricular extrasystoles, if causing undue symptoms and when not the result of extracardiac mechanisms, may occasionally be quieted with quinidine. The presence of frequent premature ventricular systoles in instances of recent myocardial infarction warrants the use of quinidine to prevent the possible occurrence of ventricular tachycardia and fatal ventricular fibrillation. Occasionally quinidine has been used intravenously in instances of ventricular tachycardia and short runs of ventricular fibrillation, but because of possible peripheral circulatory collapse and drop in blood pressure and also further depression of the conducting tissues it should be used only with great caution. Because of its action in reducing the irritability of the myocardium and in prolonging the intraventricular conduction time, the drug should not be used for patients with marked degrees of block in the conducting system. Because of its peculiar properties as enumerated, it is evident that quinidine has certain definite indications and also contraindications, and these should be fully understood before quinidine is administered.

Digitalis has certain definite known actions on the cardiac mechanism which are well stated in the standard textbooks. It is known definitely to have a selective action on the conduction system, especially the auriculoventricular node, and when used beyond therapeutic dosages it will give rise to bizarre ectopic rhythms and ultimate ventricular fibrillation if not stopped. Together with its stimulating action on the vagus nerve and depression of auriculoventricular conduction, it has been used to slow the ventricular rate and maintain it at a slow rate in auricular fibrillation. Gold and his associates have recently shown that the vagal factor predominates in such instances with moderate digitalization, while the extravagal factor predominates after larger doses. The apparent discrepancy of the action of digitalis in sinus rhythm as contrasted with auricular fibrillation in slowing the ventricular rate is not clearly understood at present. However, the presence of congestive failure, with either sinus rhythm or auricular fibrillation, is an indication for the use of digitalis. In contrast to quinidine, digitalis increases the contractility of the heart. The exact mechanism by which

digitalis does this is not fully explained at present. The one constant effect of the drug is to cause a diminution in cardiac size in normal animals and man and in patients with congestive heart failure. Some investigators have explained this as a consequence of its direct action on the myocardium with varied results. The prevailing theories are that there may be an increase in tone, an increase in systolic force or a decrease in the diastolic length of the individual muscle fibers. Others have attributed its beneficial actions to a peripheral circulatory action by pooling the venous blood in the liver channels, thus decreasing the size of the heart and allowing for more efficient contraction. Discussion of the experimental evidence is not pertinent at this time, but, whatever the exact action may be, digitalis helps to relieve congestive heart failure.

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TREATMENT OF TUBERCULOSIS IN NEGROES

***To the Editor:*—The superintendent of a tuberculosis sanatorium recently stated that collapse therapy (pneumothorax) is inadvisable when the patient is a Negro. He maintained that this is the consensus in leading tuberculosis institutions, citing in particular Bellevue Hospital in New York City. Is belonging to the Negro race now considered a contraindication to collapse therapy in pulmonary tuberculosis? Can you furnish any references on the subject?**

M.D., New York.

ANSWER.—At one time it was believed that no treatment was of any avail for Negro patients. This probably was due to the fact that Negroes usually did not report for examination until their disease was too advanced for treatment to be of any benefit. In more recent times, however, there has been much health education work done among Negroes, which has encouraged at least some of them to be examined while apparently in good health. Negro nurses and physicians are doing a great deal of this educational work. Many clinics have been established for those with little or no financial means, which have made examinations readily available. Surveys have been conducted which include examinations of healthy appearing Negroes. These and other activities have resulted in finding tuberculosis in earlier stages when symptoms are present and in the presymptom stage in many cases. Thus, large numbers of Negroes are having tuberculosis detected at a time when it is treatable.

Some workers are of the opinion that the Negro develops a different type of tuberculosis than the Caucasian—a more rapidly progressive type. They are of the opinion that this may be due to lack of immunity; others, however, contend that the Negro does not develop a different type of tuberculosis than the Caucasian but that his exposure often is of such a nature that so many tubercle bacilli are admitted to his body as to produce overwhelming and rapidly progressive disease. In either event, the Negro who does not have hopelessly advanced tuberculosis may have his lesions treated with great success and by the same methods as are employed in the treatment of the Caucasian.

Collapse therapy has been and is being used extensively in the treatment of tuberculosis among Negroes. The procedure of choice is artificial pneumothorax, but when, by reason of adhesions, this cannot be accomplished, surgical procedures, especially extrapleural thoracoplasty, are indicated and have been practiced with remarkable success.

Chadwick, Markoe and Thomas (*Am. Rev. Tuberc.* **28**:759 [Dec.] 1933) reported the results of treatment of 464 Negroes who had pulmonary tuberculosis. They were all on strict bed rest, and collapse therapy was used in 70 per cent. They divided their patients into light, medium and dark skinned groups. While the results of treatment were a little better in the light skinned group, a higher percentage of improved cases was found in the dark than in the medium group. They concluded that the degree of color is not particularly significant. They produced an excellent record for treatment among these Negroes when one considers that in 90 per cent of the patients the disease had advanced beyond the minimal stage before treatment was instituted.

Brock (*ibid.* **28**:767 [Dec.] 1933) reported the results of his collapse therapy work on thirty-six tuberculous Negro patients, all of whom were in the advanced stage of the disease when treatment was begun. Thus he started with a serious handicap. Therefore only 17 per cent were improved or restored to working capacity.

Gaines and Keller (*ibid.* **28**:779 [Dec.] 1933) also treated Negro patients by collapse therapy and came to the conclusion that the results approximate those obtained in the white race closely enough to reward the physician for his effort and the patient for his cooperation in submitting to this form of treatment. They consider artificial pneumothorax as the procedure of choice, although extrapleural thoracoplasty was used in some cases. With few exceptions they believed that the indications for collapse therapy in the Negro race should be identical with those of other races and the results obtained in their hospital compared favorably with results reported among combined races.

Since these reports were made, large numbers of Negroes have been treated by collapse therapy with excellent results. In Puerto Rico J. Rodriguez Pastor has reported (*Journal-Lancet* **60**:160 [April] 1940) that ambulatory artificial pneumothorax has been administered to more than 4,000 patients and pneumothorax has been used in large numbers of patients who are hospitalized. Negro patients receive artificial pneumothorax the same as those of other races and apparently with similar results.

Guild, who is director of the Negro program of the National Tuberculosis Association, travels extensively through the South and finds that collapse therapy is being used on Negroes in nearly all of the Southern states.

Therefore the Negro race is not now generally considered a contraindication to collapse therapy in pulmonary tuberculosis. Artificial pneumothorax is doing much not only to control tuberculous lesions in individual patients but also to convert positive sputum to negative and even prevent some patients from becoming contagious.

TOXICITY OF VINYLITE RESINS

***To the Editor:*—What are the industrial complications such as allergy and toxicity of a product used in dyeing shoes, namely "Vinylite."**

Russel G. Means, M.D., Columbus, Ohio.

ANSWER.—"Vinylite" is the trade name for a series of vinyl compounds manufactured by the Carbide and Carbon Chemicals Corporation. This type of plastic may be produced in any color or in translucent and transparent forms. It is suitable for use as articles of personal wear such as belts, suspenders, garters and shoe tops and for dentures, phonograph records and splints and in coating materials. Although no information is available on the use of this type of resin as a shoe dye, patents have been awarded for its use as a coating for textiles. This use involves the addition of ancillary products such as plasticizers, solvents, stabilizers, dyes and inhibitors, which include known skin irritants and sensitizers. Claims have been made that vinyl compounds themselves are nontoxic; however, there still remains the possibility of injury from the other products present. The type of skin injury associated with these resins was described by Dr. Erwin P. Zeisler in THE JOURNAL, June 29, page 2540, in an article which refers to dermatitis from garters and wrist watch straps made from vinyl acetate and vinyl chloride. More recently, dermatitis from handling resin-lined tin cans has been reported (Schwartz, Louis, and Russell, J. P.: Occupational Dermatitis from Handling Resin-Lined Tin Cans, THE JOURNAL, Aug. 10, 1940, p. 448).

SOLUTION OF POSTERIOR PITUITARY FOR HERPES ZOSTER

***To the Editor:*—What is the rationale for the use of solution of posterior pituitary in the treatment of herpes zoster? I am treating a white man aged 31 with daily injections of 15,000 international units of thiamine hydrochloride. He has herpes zoster involving the ophthalmic division of the trigeminal nerve. The results are apparently good, the lesions crusted after the third injection and the pain has almost disappeared. I have spoken to some men who have used Vitamin B_1 in cases of herpes zoster and they report little success. However, their dosage was lower.**

Sidney J. Kohle, M.D., Woodmere, N. Y.

ANSWER.—Somers and Pouppirt (Herpes Zoster: Some of Its Clinical Aspects, *California & West. Med.* **42**:370 [May] 1935) have formulated a theory to explain the action of solution of posterior pituitary and epinephrine in relieving the pain of herpes zoster. Because of the fact that one of the chief changes in the tissues affected in this disease is vasodilatation, they suggest that it is the vasoconstricting action of these drugs that relieves pain in many cases. They differentiate two kinds of pain in zoster: (1) a stabbing, shooting pain, usually intermittent, along the segment or segments involved, usually not sharply localized, and (2) a sharply localized burning, itching or stinging pain at the site of the skin lesions or at the locality at which they are about to appear. Solution of posterior pituitary regularly relieved pain of the second kind

but was not always successful in the neuralgic pain of the first variety, a point in which their experience agrees with that of other writers.

Pillsbury and Fondé (The Treatment of Herpes Zoster, *M. Clin. North America* **20**:239 [July] 1936) quote Somers and Pouppirt's theory and agree that it seems to them a reasonable explanation.

Flexner, Chassin and Wright in a recent article (Studies in Herpes Simplex Encephalitis in Rabbits, *J. Infect. Dis.* **66**:30 [Jan.-Feb.] 1940) tried vitamin C, sulfanilamide and pitressin in the attempt to control the encephalitis of rabbits. In discussing the possible action of pitressin, they evidently included it in their experiment because of its use in the treatment of herpes zoster and although they apparently had not read Somers and Pouppirt's article they came to the same conclusion, that the drug probably acts by its vasoconstrictive power.

PROBABLE ARTHRITIS OF WRIST

To the Editor:—A girl aged 17 has been playing golf daily during the summer months for the past four years. Last year she developed a pain in the right wrist while playing and it bothered her off and on during the remainder of the summer. Rest for a few days has always relieved the pain. During the winter she practiced on the violin one hour or more daily without experiencing the slightest discomfort in her wrist. On June 1 she began playing golf again and got along well for four or five weeks. The pain then returned and has caused her a great deal of annoyance. The pain seems to be located in the second carpometacarpal, that is, the joint between the second metacarpal and the trapezoid. On examination and questioning I have noted the following points: 1. Pain occurs on pressure on the dorsal surface of the wrist over this joint. 2. Cocking of the wrist at the top of the back swing causes pain in this region. 3. After a round of golf, flexion and extension of the wrist cause pain. 4. Pressure on the palm of the hand as, for example, leaning on the arm with the palm of the hand resting on a table, causes pain. 5. Pressing together the index finger and the thumb as in holding a pen causes pain if done one or two hours after playing a round of golf. She has been instructed by three well known professionals and her form is considered good. An improper grip or faulty swing can probably be ruled out as a cause of the trouble. What can the cause of this pain be and what can be done to relieve it permanently?

M.D., West Virginia.

ANSWER.—The history suggests an arthritis. Presumably x-ray films have been made and carefully studied, although this is not mentioned in the letter. If the trapezoid and second metatarsal joint are clear and show no changes, it would be well to scrutinize closely the x-ray film of the proximal row of carpal bones of the wrist, paying particular attention to the semilunar bone, which occasionally is the seat of a noninfectious aseptic osteitis called Kienböck's disease.

All foci of infection should be searched for and eliminated. If the condition is an arthritis, rest is essential, even to the extent of giving up golf for a season. A cock-up wrist splint may be worn, which will keep at rest the various component joints of the wrist and still permit movement of the fingers. If this fails to give relief, consultation with an orthopedic surgeon would be advisable.

THUMB SUCKING IN INFANTS

To the Editor:—What is the attitude of pediatricians toward thumb sucking in infants and children? Should one attempt to stop them or let the habit run its course? Is it thought that dentition and oral development are influenced by thumb sucking?

W. E. Oldham, M.D., Lebanon, Ky.

ANSWER.—The opinion of pediatricians is somewhat divided with regard to the proper handling of thumb sucking. Some believe that the habit should be completely ignored in all infants under a year of age. Others favor the use of some restraining device, such as pasteboard splints on the arms, aluminum mitts or other coverings for the hands. The application to the thumb of bitter substances is of service only in the milder cases and even in such instances may not be of benefit.

Few pediatricians are willing to accept the view that thumb sucking may have a sexual basis. Curtailment of the thumb sucking may lead to the development of some substitute habit. Thumb sucking is more liable to occur when a child is about to go to sleep or when he is hungry.

Opinions seem equally divided as to the effects of thumb sucking. Some orthodontists are inclined to believe that the continued sucking will lead to malocclusion and deformity of the jaw; others do not concur but rather consider the etiology of malocclusion to be based on heredity and other factors.

If the habit is unduly frequent or of a combined type, that is, accompanied by hair pulling, nose rubbing and the like, it is probable that efforts should be made to overcome the habit. Mechanical restraint probably is the most effective method of treatment in such cases. In milder cases in which the habit is of infrequent occurrence, it may well be ignored.

SYPHILITIC MYELITIS

To the Editor:—A white woman aged 56 complained on March 5, 1940, of paresthesias of the feet, legs and lower part of the abdomen. There was a burning sensation in the right foot beginning at the plantar surface of the second toe and running back along the medial half of the plantar surface of the foot and up the leg. There was a feeling of tightness about the lower part of the abdomen and back. With the onset of these symptoms in January 1940 there was difficulty in walking. The sensory disturbances were distressing at night. She had lost 10 pounds (4.5 Kg.) since the onset of her illness. The patient is intelligent and there is no loss of memory. Speech is not affected. There are no headaches, vertigo, or gastrointestinal complaints. The appetite is good. Menstruation ceased at the age of 51. Her past medical history is negative. She has been married for thirty-one years, has never been pregnant, and states that her husband, aged 71, is in good health. The patient weighs 105 pounds (47.6 Kg.). There are no abnormalities of the skin, eyes, ears, nose, throat or lungs. The pulse rate is 84. The blood pressure is 176 systolic, 90 diastolic. Abdominal and pelvic examinations are negative. The gait is unbalanced, faltering and ataxic. Falling is apt to occur if a cane is not used. The pupils react normally to light and in accommodation. The patient's eyes were examined by an ophthalmologist and no abnormalities whatever were detected. There is no tremor. The tendon reflexes at the wrist and elbow are normal. The superficial abdominal reflexes are absent. The knee jerks are hyperactive. The Babinski reflex is questionable. The Romberg test is positive. The finger to nose test is well done. The heel to knee test cannot be evaluated because of spasticity of both lower extremities (adductor spasm?). Thermal and tactile sensibility is impaired in both lower extremities. The degree of impairment increasing from above downward. The urine is normal. On March 18 the red blood cells numbered 3,510,000, the hemoglobin 80 (Sahli), white blood cells 9,750, the differential normal. The blood Kahn reaction March 18 was positive. Spinal fluid examination March 29 revealed normal pressure, the Wassermann and Kahn reactions negative, white cells 4, globulins moderately increased, total protein 150 mg., colloidal gold curve 11222210000. My diagnosis was neurosyphilis with early myelitis involving the lower dorsal and lumbar regions of the cord. Since March 30 she has received ten injections of bismuth subsalicylate in oil followed by ten 2 Gm. doses of tryparsamide and is now on a second course of the bismuth compound. She is taking potassium iodide orally (60 minims, or 3.7 cc., of the saturated solution daily) and tolerates her treatment well. To date there has been no improvement in her nervous symptoms, although there is no evidence of progression. The positive neurologic signs remain the same. The weight remains the same. A red blood cell count repeated on July 11 showed 4,040,000 with a hemoglobin of 88 per cent. Blood tests repeated at another laboratory July 15 revealed the Wassermann negative, Kahn 4 plus and Kline 3 plus. I would appreciate your opinion as to the diagnosis. I understand syphilitic myelitis to be a diffuse meningovascular lesion of the cord with general softening, amounting to infarction. The clinical and laboratory observations in this case seem to fit this diagnosis, except for the normal spinal fluid cell count, which would speak against meningeal involvement. What treatment would you advise? What is the prognosis? What of fever therapy in this case, and when should it be given with reference to drug treatment?

M.D., Ohio.

ANSWER.—From the description, the patient's condition may be classified as a myelopathy or a myelitis; or, in view of the serologic test, the possibility of a vascular type of neurosyphilis must also be considered. A report of the jugular compression test and a report of x-ray examination of the thoracic spine would be of help in making a diagnosis. The first blood count report raised the question of a pernicious anemia, so further study of blood smears and a gastric analysis with histamine may be helpful.

The results of treatment of patients who have a syphilitic myelitis are quite unsatisfactory. In view of the patient's age and type of involvement, the continued use of tryparsamide and a bismuth compound would seem warranted. The use of fever therapy in this type of case is attended with considerable risk and small chance of improvement.

ARTHRITIS OR SERUM ARTHRALGIA

To the Editor:—A man aged 45 had no joint symptoms until he was given serum for pneumonia in February 1940. He developed a serum sickness and continues to have stiffness and pain in practically all his joints. The joints are not deformed but are tender. Warm baths and salicylates have been of no value. Can you suggest any treatment that might help? There are no evident foci and he is otherwise in good health.

M.D., Indiana.

ANSWER.—It is unlikely that articular symptoms of several months' duration are related to serum therapy. The articular symptoms of serum sickness generally last not more than a few days, in the experience of Boots and Swift, not more than nine days in any one joint. In serum sickness there occur, two or three weeks after the serum therapy, fever, urticaria, sometimes enlargement of lymph nodes and, in many cases, pain and tenderness of the joints, less often actual redness and swelling of joints. Arthralgia, rather than arthritis, is usually present. Analysis of the synovial fluid may reveal an increased cell count and the presence of the offending antigen.

In view of the persistence of the patient's pains, he apparently has some condition other than the arthralgia of serum sickness. He is approaching the age when degenerative (hypertrophic)

arthritis and its accompanying muscular stiffness are common. The latter generally can be readily differentiated from chronic atrophic (infectious) arthritis by making roentgenograms and estimating the sedimentation rate.

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UNUSUAL SYMPTOMATOLOGY IN PERIARTERITIS NODOSA

To the Editor:—**A woman aged 40, single, with a definite diagnosis of periarteritis nodosa, was given an ampule of metaphyllin 0.24 Gm. in a 10 cc. solution intravenously. Two and a half hours later she became disoriented and failed to respond to questions, repeating "vomit, vomit" and sucking on her fingers. There is a question of a temporary amaurosis. The left pupil reacted to light (the right dilated and fixed from a previous episode of retinal hemorrhage and blindness). Physical examination was otherwise negative. One hour later I was called because of a clonic convulsion with frothing at the mouth and coma. There was no bowel or bladder incontinence. The pulse was full and bounding. There were no sibilant or sonorous rales, which had been present for years on and off and which were noted early that morning. Nikethamide was given intramuscularly. Slow and irregular respiratoins soon appeared, to become deeper and more regular. One and a half hours later I returned because of another similar convulsion. The condition was as before. Nikethamide was given again. The patient remained comatose for another two hours. At that time she stirred and turned on her side. She looked up, recognized me and spoke to me. There were still moist rales in her chest. She was still disoriented. Four hours later she responded to questions and made plans for her family and for her own diet for the following day. She thought she "was dry" but didn't care for any food that night although she sipped a little water. She slept well through the night. The following morning her appetite was poor. She felt exhausted. She had vomited some orange juice. Sibilant rales were noted throughout both lungs. There was an equivocal Babinski sign on the left and a weak left ankle jerk. The abdominal reflexes were lively except for the lower left quadrant. She remembered nothing since a faintness coming over her the previous day at the beginning of the episode until seeing me some eight hours later. The blood pressure was now 132/80 (from 170/94 of the previous day). She has been taking epinephrine, iodides, ephedrine, bromides and metaphyllin (by vein) as necessity required for a number of years. For the last month there has been slight weekly vaginal bleeding, which this day was more profuse (this has occurred previously after metaphyllin). For a number of days there has been numbness of the toes relieved by heat and elevation, and which is now gone. Is it possible to tell me what occurred? No air, I am sure, was injected. I would not care to use the drug again if there is any relationship, but she feels that it has always helped her in the past.**

M.D., Connecticut.

ANSWER.—It seems unlikely that the drug was responsible for the train of symptoms described in this case. Metaphyllin is theophylline with ethelenediamine. Less than 0.2 Gm. of theophyllin is contained in 0.24 Gm. of the compound. This dose is well within the limits of safety, especially if the injection is given rather slowly. From one and one half to two minutes should be consumed in injecting the drug. The fact that the patient had received many such injections previously would rule out sensitiveness to the drug. In addition to this, patients who are sensitive react promptly and not two and a half hours later.

In a disease with such protean manifestations as periarteritis nodosa it is much more likely that the symptoms described were the result of the disease itself, probably a cerebral thrombosis or the rupture of a cerebral aneurysm.

DEPILATORY PASTE

To the Editor:—**Is there any contraindicatioa to the use of a depilatory paste containing barium sulfide on the face, the paste containing 4 drachms (15 Gm.) of barium sulfide and 2 drachms (8 Gm.) each of powdered zinc oxide and powdered starch? Is it advisable to reduce the average exposure time of from one to two minutes if such a paste is used on the face?**

M.D., Illinois.

ANSWER.—The depilatory paste mentioned is one of the formulas of Duhring and must be thinly applied to the area to be treated and allowed to remain until there is a slight sensation of burning (not longer than one or two minutes) and then scraped off. Such a paste when used repeatedly on the face is apt to cause dermatitis and conjunctival irritation, in addition to being unpleasant to the sense of smell because of its sulfide content. Since the process must be repeated with the reappearance of the hairs, there is great likelihood of irritation (dermatitis venenata) on the face, and it is well, therefore, to reduce the exposure time to a minimum. Other methods of depilation, e. g. electrolysis, in proper hands is a safer and more permanent procedure for removing superfluous hair if the involvement is not too extensive.

STERILIZING ADHESIVE TAPE

To the Editor:—**I have the problem of sterilizing adhesive tape which may not be put to immediate use but which may have to be stored for several months. Can you tell me what method I can use without impairing the adhesive qualities of the tape? Will exposure to short wave diathermy kill bacteria unless there is sufficient heat developed to affect also the sticking power of the adhesive? If so, what wavelength would be most effective?**

M.D., New York.

ANSWER.—Exposure to short waves is at best an uncertain method of sterilization of adhesive tape, and subsequent packing for storage would add to the technical difficulties involved. Sterilization with moist heat is the method of choice. One firm of manufacturers (Johnson and Johnson, New Brunswick, N. J.) produces a tape which, it is stated, may be so treated without impairment of its adhesive qualities. Sterilizable tape should be faced, it is said, with crinoline or some other cloth. It must be so placed in the autoclave that steam can freely reach the entire surface; i. e., it should lie in separated flat strips or sheets or in a loose roll. The manufacturers recommend 10 pounds pressure (240 F.) for thirty minutes. A minor problem is to prevent excessive drying during the period of storage, which would impair the adhesive quality.

FUNCTIONAL POSITION IN ANKYLOSIS OF THE HIPS

To the Editor:—**What is the optimal functional position in bilateral ankylosis of the hips?**

M.D., Pennsylvania.

ANSWER.—Abduction of from 10 to 15 degrees of each leg with slightest degree of external rotation probably would be considered best in the average case. This produces the broadest base of support for walking. There are some instances in which one must give consideration to the individual case; namely, some people would rather have the hips stiff in flexion so that they can sit, rather than in extension, which is better for standing, walking and lying. A court reporter may prefer the sitting position.

Another factor is the amount of movement possible in the lumbosacral area. Unfortunately so many victims of bilateral ankylosis have in addition ankylosis of the sacro-iliac and lumbosacral joints that they have no outlet in the lower back area to compensate in any measure whatever for the stiffness of their hips. Occupation and marital relations are important factors.

DYSMENORRHEA AND ARTIFICIAL MENOPAUSE

To the Editor:—**A woman aged 36, married twelve years, with no children (she has never used contraceptives), has always had severe menstrual pain. In fact, no medication ever gave relief until about one year ago, when I started giving pantopon hypodermically. This seemed justified in view of the excruciating pain and of the fact that it is given only once a month. The effectiveness of pantopon is still as great as a year ago and she does not suffer nearly as much. Now this patient wants my opinion as to x-ray treatments for a therapeutic menopause. She argues that the chances of her having children are slight at this age after twelve years of sterility and that her life from now till the natural menopause would certainly be much happier without the dreaded periods. Would the symptoms of the menopause induced by irradiation differ at all from the symptoms of a natural menopause? Is the effect on sexual desire any different? I have studied this particular case for several years and have tried everything recommended for dysmenorrhea, including progesterone, chorionic gonadotropin and even a dilation and curettement, which was recommended by a gynecologist in consultation. All these were ineffectual. So I am anxious for an opinion on the effect of x-ray treatments.**

M.D., New York.

ANSWER.—The symptoms of the menopause induced by roentgen or radium therapy are similar to and ordinarily not notably more severe than those of the natural menopause. There is persistence of satisfactory libido in nearly one half of the cases, although some decreased desire is to be anticipated.

In a case such as this, at the age of 36, most gynecologists would advise strongly against induction of an artificial menopause. An abdominal operation with removal of the menstruating portion of the uterus or resection of the presacral nerve would be the procedure of choice, provided palliative measures fail to bring comfort.

The following dysmenorrhea regimen merits a trial:

Beginning three days before the expected onset of pain or menstruation, the patient should be outdoors as much as possible, be on a sparing diet, keep the bowels free and take 1 teaspoon of elixir of phenobarbital three times daily. With onset of pain or menstruation the patient should rest quietly, double the dosage of elixir of phenobarbital and take one-half grain (0.03 Gm.) of codeine sulfate every half hour until relief, not in excess of six tablets in twenty-four hours.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, December 21, page 2203.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, February 10-12. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Part II, Cleveland, May 31-June 1. Final date for filing application is April 1. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Parts 1-A and 1-B, Feb. 17. Final date for filing application is Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Part II, Groups A and B, Cleveland, May 28-June 1. Final date for filing application is March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Cleveland, May or June. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written.* Cleveland, June 1-2. Final date for filing application is May 1. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, March 30-31, following the Region I meeting of the American Academy of Pediatrics. Chicago, May 18, following the Region III meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY. *Oral.* Cleveland, May 30-June 1. Final date for filing application is April 15. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

Rhode Island July Report

Dr. Robert M. Lord, secretary, Division of Examiners, reports the oral and written examination for medical licensure held at Providence, July 11-12, 1940. The examination covered 8 subjects and included 75 questions. An average of 80 per cent was required to pass. Nine candidates were examined, all of whom passed. One physician was licensed to practice medicine by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1938)	83
Johns Hopkins University School of Medicine		(1920)	83
St. Louis University School of Medicine		(1939)	89.5
Hahnemann Medical College and Hospital of Philadelphia		(1939)	80, 85, 85, 88
McGill University Faculty of Medicine		(1938)	86
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1937)	88.2

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Boston University School of Medicine		(1938)	N. B. M. Ex.

California June Report

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination for medical licensure held at San Francisco, June 25-27, 1940. The examination covered 9 subjects and included 90 questions. An average of 75 per cent was required to pass. One hundred and sixty-three candidates were examined, 155 of whom passed and 8 failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1940)	77.2, 79.1, 80.9, 84
Stanford University School of Medicine		(1939)	85.3,
	(1940) 76.2, 76.4, 76.7, 77.6, 79.3, 79.4, 79.8, 80, 80.1, 80.3, 80.6, 81.2, 81.2, 81.8, 82, 82.3, 82.7, 82.8, 83.3, 83.8, 84.2, 84.2, 84.3, 84.8, 85.2, 85.3, 85.7, 85.8, 85.9, 86, 86.1, 86.2, 86.3, 86.6, 86.8, 86.9, 87.4, 87.7, 88.1, 88.2, 89.8, 91.2, 92.1		
University of California Medical School		(1940)	75.7,
	75.9, 77.7, 79.1, 79.8, 80.1, 80.7, 81.8, 82.1, 82.2, 82.2, 82.3, 82.6, 82.6, 83, 83.1, 83.9, 84.3, 84.3, 84.3, 84.4, 84.6, 84.6, 85, 85.1, 85.1, 85.4, 85.4, 85.4, 85.6, 85.6, 85.7, 86.3, 86.4, 86.4, 86.4, 86.7, 87.2, 87.9, 88.2, 88.3, 88.8, 90.1, 90.2, 91.6		
University of Southern California School of Medicine		(1940)	77.7,
	81.7, 85.4, 85.7, 86.3, 90.3		
Loyola University School of Medicine		(1940)	85.7
Northwestern University Medical School		(1940)	83,
	86.1, 88.9, 89.1, 89.2		
Rush Medical College		(1938)	82.9
University of Illinois College of Medicine		(1940)	79.1
University of Louisville School of Medicine		(1940)	88.4
Louisiana State University School of Medicine		(1940)	83.6
Johns Hopkins University School of Medicine		(1936)	80.4,
	(1937) 80.7		
St. Louis University School of Medicine		(1940)	75.3, 77.1,
	79.4, 79.7		
Creighton University School of Medicine		(1938)	81.4,
	(1939) 76.3, 77.3, 78.7, 78.7, 84.6		
University of Nebraska College of Medicine		(1939)	78
Columbia University College of Physicians and Surgeons		(1940)	81.3, 82.2, 88.1, 88.8
Cornell University Medical College		(1939)	80.4
University of Oregon Medical School		(1939)	80.4
Hahnemann Med. College and Hospital of Philadelphia		(1939)	75.6
University of Pennsylvania School of Medicine		(1939)	78.1
Marquette University School of Medicine		(1940)	83.1, 84.3
University of Wisconsin Medical School		(1939)	79.6
Queen's University Faculty of Medicine		(1938)	76.1
University of Toronto Faculty of Medicine		(1935)	87.4
McGill University Faculty of Medicine		(1936)	77, 77.4, 84.3,
	(1937) 84, (1939) 83.7, (1940) 79, 87.7		
Medizinische Fakultät der Universität Wien		(1913)	77.9,
	(1937) 79.7, 86.7		
University of Oxford School of Medicine		(1930)	87.2
Christian-Albrechts-Universität Medizinische Fakultät, Kiel		(1911)	78
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1929)	75.6, (1932) 79.2
Hamburgische Universität Medizinische Fakultät		(1923)	75.9
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1908)	76.1
Thüringische Landesuniversität Medizinische Fakultät, Jena		(1921)	76.1
Universität Heidelberg Medizinische Fakultät		(1911)	99.4
Regia Università degli Studi di Firenza. Facoltà di Medicina e Chirurgia		(1912)	82.9

School	FAILED	Year Grad.	Number Failed
University of California Medical School		(1939)	1
Chicago Medical School		(1928)	1
Rush Medical College		(1938), (1939)	2
University of Minnesota Medical School		(1940)	1
University of Cincinnati College of Medicine		(1940)	1
Marquette University School of Medicine		(1940)	1
McGill University Faculty of Medicine		(1940)	1

Book Notices

The Diagnosis and Treatment of Cardiovascular Disease. Edited by William D. Stroud, B.S., M.D., F.A.C.P., Professor of Cardiology, University of Pennsylvania Graduate School of Medicine, Philadelphia. Volumes I and II. Fabrikoid. Price, $18, per set. Pp. 801; 1001-1825, with illustrations. Philadelphia: F. A. Davis Company, 1940.

This is a moumental contribution to the field of diseases of the heart and blood vessels. It covers the modern point of view fully. This is important, since the subject has undergone considerable change in the past two decades as regards (1) the aspects of cardiovascular fields emphasized, (2) the substitution of the functional for the purely morphologic point of view. These changes are clearly reflected in this treatise. The sixty-two chapters of this two volume textbook are contributed by fifty-six eminent American authorities, the majority of whom have themselves advanced the knowledge of the subdivision about which they write. Being, almost without exception, clinicians as well as investigators, they write from the practical side based on experience in handling patients. They have thus presented the practical information for diagnosis and therapy in addition to the general concepts of diseases of the heart and blood vessels. The influence of the American Heart Association, in which many of the authors have taken a leading part, is evident throughout the book, and it is crystallized in the chapter on the public health aspects of heart disease contributed by Marvin.

An idea of the scope of the volume can best be appraised by an enumeration of the various contributions (space does not permit much more in this review).

The introduction, written by Sprague and P. D. White, orients the reader with regard to the prevailing emphasis of the various aspects of the subject. Maude Abbott presents a brilliant summary of congenital anomalies. Rheumatic heart disease is covered in three chapters contributed by McEwen, Paul and Duckett Jones. Bacterial endocarditis is reviewed by William Dock; cardiovascular syphilis is covered in two chapters by Paullin and Minnich and by Stokes and Anderson. L. A. Conner reviews the subject of cardiac neuroses, Porter the effects of anemia and Durant that of pulmonary diseases. The interrelation of the kidneys and the cardiovascular system is beautifully

handled by Hayman. Barr has summarized the relationship of diseases of the endocrine system and the circulation, and Thomas the relationship of hyperthyroid activity and the heart. Soma Weiss presents an excellent review of the effects of nutritional deficiency diseases on the heart. Barber contributes the chapter on trauma, Porter and P. D. White the chapters on pericarditis, Roesler the one on cardiac enlargement, Vander Veer the one on chronic valvular heart disease and Fred Smith, Robert Lévy and Stroud the three chapters on coronary artery disease and angina pectoris. Bellet summarizes the subject of the blood supply of the heart, King the normal heart, Wolferth and Margolies the subject of heart sounds, Wilson, and Bellet and McMillan the field of electrocardiography, Margolies the field of roentgenography, Herrmann the subject of cardiac arrhythmia, and Bromer and Stroud the conditions of congestive heart failure and left heart failure (and paroxysmal cardiac dyspnea).

The general management of the cardiac patient is dealt with separately by several contributions: on digitalis by Stroud and Vander Veer, and by McMillan and Bellet, on quinidine by Kerr, on physical and spa therapy by Comstock and Stroud, and on rehabilitation in industry by Stroud. Surgery and pregnancy in the cardiac patient are amply discussed by Levine. The surgical treatment of heart disorders is reviewed by Beck, with special chapters on alcohol nerve block in angina pectoris by Grant and on total thyroidectomy by Blumgart and Riseman.

The subject of peripheral vascular diseases is begun by a consideration of normal blood pressure by E. V. Allen, of capillary circulation by DeGraff and Kossmann, and of venous pressure by Schleiter. Shock is presented by Freeman, hypertension by Stieglitz and by Houston, low arterial pressure by J. H. Barach, arteriosclerosis by Eli Moschcowitz, periarteritis nodosa by Farley, thrombo-angiitis obliterans by Buerger, erythromelalgia, lymphedema and sudden vascular occlusion by E. V. Allen, thrombophlebitis by N. W. Barker, aneurysm and auriculoventricular fistula by Hines, arteriosclerosis obliterans, acrocyanosis and Raynaud's syndrome by I. S. Wright, and vascular anomalies and varicose veins by de Takats. An excellent article on edema by Landis concludes the book.

From the foregoing outline it is obvious that some reduplication is unavoidable, but the extent of reduplication present in this book could have been considerably curtailed by judicious editorial deletions, and this would have improved the treatise and considerably abbreviated it. The fault inherent in any volume contributed by many authors is that the style is variable, and this is true in the present work. It is, however, unavoidable. There is the advantage of range of appeal, which satisfies various readers. Readers ranging from the medical student to the specialist in cardiovascular diseases will find much in this book which will interest them. The profuse use of illustrations, case reports, selected bibliographies and an excellent index enhance the value of the book. It is regrettable that in the final proofing the fact was overlooked that a few of the illustrations were upside down and that singular instead of plural reference to their own opinion was used in one of the chapters by the joint authors. By virtue of the division of topics discussed, some topics, for example myxedema heart, have been omitted. Considerable improvement might also have been attained in the book by a better arrangement of the sequence of the chapters and by subdividing it into major sections. The innovation of showing engravings and short biographies of the men who have made the milestones in cardiovascular diseases is appealing, especially since the engravings themselves are so excellently executed.

This treatise is a splendid cooperative effort and it should be in the library of every one who is interested in the subject of cardiovascular diseases. The reviewer can recommend the book no better than Sir Thomas Lewis, who in the foreword states: "The brilliant list of American authors of the present contents includes a score of names known in every part of the world where cardiovascular diseases have been intensively studied; they are known for the solid contribution of those who bear them to their subject. Rarely before has such a number of authoritative writers combined to place its views of a branch of medicine on record, and never before of cardiovascular disease; it is a guaranty to the reader that he is in direct or close contact with all the fountains of modern knowledge, the most important guaranty perhaps that any reader can be given."

Der klinische Blick. Von Prof. Dr. Erwin Risak. Third edition. Paper. Price, 6.60 marks. Pp. 230. Vienna: Julius Springer, 1940.

Dr. Risak presents no new or startling discoveries. He merely presents a careful survey of objective clinical phenomena that are readily observable when the physician makes use of his five senses. He leads the reader on to the interpretation and coordination of these observations, proceeds to the development of what should be the birthright of every true clinician, namely insight or what is at times called clinical intuition, the ability rapidly to evaluate the importance of seemingly widely different phenomena, and to fit them into the harmonious picture of clinical syndrome or disease entity. A pupil of the school of von Hochenegg and Chvostek, and remotely of Bamberger, Skoda and Auenbruegger, Dr. Risak comes to this approach quite naturally and his contribution is useful. Particularly in this day when medicine in Europe must be practiced in mass, the capable clinician must have the ability to sort his material rapidly but surely. It is here that clinical insight, the "clinical eye," is of utmost value. Risak would by no means have the accessory laboratory aids or the use of the modern diagnostic armamentarium neglected, but he is quite right in stressing the significance of the art of medicine as an important though often neglected phase in our modern medical training. The book is well ordered. The first part concerns the physician, the second part the environment of the patient, and the third part, of approximately 150 pages, the phenomena to be observed in the patient. The presentation is both thorough and instructive but sufficiently informal and personal to be entertaining as well. Shrewd clinical observations illustrate and enliven the significant points, all of which have been selected from a practical point of view. It is to be regretted that nothing quite comparable to this little volume has appeared in the more recent American literature.

A Pioneer Doctor in Old Japan: The Story of John C. Berry, M.D. By Katherine Fiske Berry. Cloth. Price, $2.50. Pp. 247, with 21 illustrations. New York, London & Edinburgh: Fleming H. Revell Company, 1940.

Dr. John Cutting Berry went to Japan in 1872 when he was 25 years old. He was the type of medical missionary who has done probably more for good will between Eastern and Western civilization than has any other pursuit. The Japanese published in their own language a short biography of his life, the first ever written about an American by the Japanese. Dr. Berry was decorated by the Japanese emperor and was hailed by the Japanese as the father of prison reform and social service work in their country. At the time of the celebration of the golden wedding of Dr. Berry the Japanese presented him with a marvelous Japanese vase; there were messages from innumerable Japanese leaders.

In the course of his medical education Dr. Berry studied under W. W. Keen and S. Weir Mitchell. He took also some lectures under Oliver Wendell Holmes. The writer has a fine sense of humor and intersperses her story with innumerable anecdotes. There are excellent pictures of Japanese civilization.

After leaving Japan in 1894 Dr. Berry settled in Worcester, Mass., as a specialist in diseases of the eye, ear, nose and throat. He practiced medicine until his eighty-eighth year. In 1918 he was appointed head of an American board to survey conditions in Japan. Thus he lived a long and useful life which was well worthy of the sympathetic record now available in this book.

Mucous Colitis: A Psychological Medical Study of Sixty Cases. By Benjamin V. White, M.D., Stanley Cobb, M.D., and Chester M. Jones, M.D. Psychosomatic Medicine Monograph I. Published with the Sponsorship of the Committee on Problems of Neurotic Behavior, Division of Anthropology and Psychology. Paper. Price, $2. Pp. 103, with 30 illustrations. Washington, D. C.: National Research Council, 1939.

For years many gastro-enterologists have felt that the term "mucous colitis" is undesirable because in this disease the colon itself is normal and the distress is due only to nervous stimuli arising in a tired or psychopathic brain. Under the circumstances it seems unfortunate that the writers of this valuable little monograph decided to retain the term "colitis." Since the genitive ending itis, which meant originally "disease of a part," has come to mean in both the popular and the medical mind "inflammation," it seems wrong to use it in describing a disease in which the organ involved is not inflamed or ulcerated. The use of the term is particularly unfortunate when there is such a disease as true ulcerative colitis and patients are constantly

being confused. They get the idea that they have a serious and fatal disease and naturally become frightened. The remarkable contribution of White, Cobb and Jones is the demonstration now that, by injecting into healthy students a drug of the acetylcholine type which produces reactions similar to those of stimulation of the parasympathetic nerves, one can produce changes in the mucosa of the bowel which somewhat resemble those seen during an attack of mucous colic. Every gastro-enterologist will want to have a copy of this monograph within reach of his desk.

Berkeley Moynihan, Surgeon. By Donald Bateman. With a preface by Lord Moynihan. Cloth. Price, $4. Pp. 354, with 8 illustrations. New York: Macmillan Company, 1940.

Unquestionably during his career Berkeley Moynihan was the most famed of all British surgeons. He was a frequent visitor to the United States and was the personal friend of many a great American surgeon. His biography has now been made available by Dr. Donald Bateman, who traces the life of the famous surgeon, describing his birth and his parenthood. Berkeley Moynihan derived many of his characteristics from a remarkable father and mother. Then came the decision as to whether or not the boy at the age of 15 would be developed for a military career or a career in medicine. He made his own choice and entered medical school in 1883. He had a retentive memory and great strength. He had planned after he entered medicine to join the army medical service but he came to the attention of the surgeon McGill and became a dresser. After graduation he was, however, appointed to become house surgeon for Mayo-Robson. Then comes an intimate account of the life of Moynihan as a young doctor and of his marriage. In 1914 the outbreak of the great war interrupted his work but gave him opportunity for fame. His first visit to the United States was in 1903, at which time he spoke at the College of Physicians of Philadelphia, discussing a paper by Dr. William J. Mayo on "Surgery of the Stomach and Duodenum." Following his return from America he introduced the use of rubber gloves and of the white coat into his surgery. It is interesting to read that because of this he was the subject of much ridicule. In the course of his development he practiced constantly the tying of knots and developed his manual skill. At the age of 40 he found himself being occasionally invited to speak in public and he soon developed a gift for witty and felicitous oratory. This accomplishment also played a great part in his advancement both in science and in public life. In July 1917 he again visited the United States in connection with our preparation for entrance into the World War. This volume makes available some of the best paragraphs from the many addresses which he made at that time in America and also provides some of his letters to his wife which discuss those travels. These are among the most interesting and valuable contributions in the book. The volume continues to trace the career of the great surgeon to the time of his death and affords many interesting sidelights on his career. It is readable and inspiring, picturing the great surgeon more as a man than as a scientist. It may well be added to the number of inspiring biographies now available in the field of medicine. If there is any criticism of the work, it is the absence of an index.

Sex in Development: A Study of the Growth and Development of the Emotional and Sexual Aspects of Personality Together with Physiological, Anatomical, and Medical Information on a Group of 153 Normal Women and 142 Female Psychiatric Patients. By Carney Landis et al. With a foreword by Nolan D. C. Lewis. Cloth. Price, $3.75. Pp. 329. New York & London: Paul B. Hoeber, Inc., 1940.

Here is the report of a research carried out under the auspices of a special committee of the National Research Council. Some 295 women were interviewed as to their sex life. They had physical and gynecologic examinations, and a number of experts in the field of sex study took part in an analysis of the results. It was, of course, impossible to submit each one of these women to a psychoanalysis. The method was instead the study and tabulation of material from medical and psychiatric case histories and reports. Each person interviewed was presented with a series of cards. Each card contained a single question. The answers were recorded verbatim. Next came an interview with questions concerning the facts and fantasies related to psychosexual development. The interview was supplemented by two questionnaires, one dealing with vocational interest and the other with a marriage inventory. Then came physical examination, roentgenologic studies of the pelvis and a psychiatric case history. The work is divided into chapters dealing with adolescence, adult sex practices, marriage adjustments, course of development, psychiatric studies of normal women, homo-erotic women, unhappily married women and psychopathologic personalities.

The evidence developed indicates that psychosexuality has its origins long before puberty. The way in which sex knowledge is gained seems to affect later attitudes. The child who has many illnesses or who is continually sick frequently exhibits difficulties in personal adjustment in adult life. The most important problem which a girl faces in adolescence is that of freeing herself from family ties. The onset of menstruation does not seem to have any radical effects in personality formation. Masturbation is a common practice which usually disappears without untoward effects on the personality. One woman in every four interviewed had sexual intercourse before marriage, with a higher percentage among girls with native born parents than among girls with foreign born parents. Apparently the determination of sexual intercourse before marriage depends in part on the standards of the social group to which she belongs, her psychology and her physical attractiveness. The evidence showed that one wife out of every three is sexually maladjusted. These and many other facts became apparent from the psychologic aspects of this study. From a physical point of view there were surprisingly few anatomic or physiologic differences between normal woman and those who suffered from functional or mental disturbances. Tendencies toward the male body form were found associated with homo-eroticism. The chief finding was the observation that the neurotic personality represents a style of life which is consistent from an early age. The volume is supplemented with samples of the examination forms that were used, tabular data, an extensive bibliography and a good index.

The International Medical Annual: A Year Book of Treatment and Practitioner's Index. Edited by H. Letheby Tidy, M.A., M.D., F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc. Fifty-Eighth Year, 1940. Cloth. Price, $6. Pp. 545, with 127 illustrations. Baltimore: William Wood & Company, 1940.

This work is now in its fifty-eighth year. It is a compilation of contributions by a considerable number of British physicians who, through a system of abstracts of recent medical literature, keep knowledge up to date. The book is compiled on an alphabetical basis. It is freely illustrated and has an adequate index for ready reference. As a compilation of the literature of the previous year, with particular reference to the British point of view, it may be unhesitatingly recommended.

Tratado de enfermedades nerviosas. Por Luis Barraquer Ferré, Ignacio de Gispert Cruz y Emilio Castañer Vendrell, jefe y auxiliares respectivamente del Departamento de neurologia del Hospital de la Santa Cruz y San Pablo de Barcelona. Tomos I y II. Cloth. Pp. 1,154, with 448 illustrations; 1,108, with 396 illustrations. Barcelona & Buenos Aires: Salvat Editores, S. A., 1936, 1940.

These two large volumes are said to be based mainly on the clinic and teachings of Dr. L. Barraquer Roviralta of the Hospital de la Santa Cruz y San Pablo de Barcelona, to whom it is dedicated. The preface by Pierre Marie is worthy of Mark Twain. After a brief historical sketch which is hardly more than a list of names the authors begin with a discussion of the methods of examination, which is adequate although physiologic observations are interspersed in a manner more confusing than illuminating. This section covers 270 pages.

The treatise proper begins with a section on the peripheral somatic nerves, which is good; the discussions are brief and generally accurate and there in an excellent description of the polyneuritis of leprosy. Nothing is said of the possibility that avitaminosis may play a role in the causation of alcoholic polyneuritis. The authors state that paralysis of the glossopharyngeal nerve causes dysphagia, a statement not confirmed by the results of surgical section of that nerve. Experience gained in the Spanish war is clearly reflected in the discussion on wounds of the nerves of the extremities. The brief remarks concerning tumors of the peripheral nerves are inadequate. Proper advice is given concerning the surgical treatment of various neuralgias.

The second and much longer section of the treatise concerning diseases of the spinal cord begins with a brief and unrelated sketch of the histology and histopathology of the central nervous

system. Then follows a short discussion of the anatomy and physiology of the spinal cord, after which the various diseases follow in encyclopedic fashion, each one being discussed in all its phases, including pathology. One notes an unusual chapter on echinococcus in the spinal canal. The second volume begins with 197 pages on the sympathetic nervous system in which American work is quoted at second hand if at all. Then follows a chapter on disorders of the extrapyramidal system, as though they had nothing to do with the brain.

The third section of the treatise deals with the diseases of the brain; extrapyramidal diseases such as Parkinson's disease and Wilson's disease were dealt with before. The discussions of cerebral diseases follow the same lines as do those of the spinal cord; after an anatomic introduction and short chapters on aphasia and apraxia the various diseases are taken up one by one and discussed from every point of view. The discussion of brain tumors occupies 140 pages and again one has the impression that American work is quoted at second hand (no bibliography is appended to this treatise).

The work is well illustrated with many interesting original photographs. One gains the impression that the authors are thoroughly familiar only with French neurology. Recent medical advances, such as quinine for myotonia congenita or potassium for periodic family paralysis, are not mentioned. The work is a compilation, doubtless useful in Spain; but the North American neurologist, with Wilson's masterpiece at his disposal, will rarely find need to consult it.

The Art of Useful Writing. By Walter B. Pitkin, Professor in Journalism, Columbia University, New York. Cloth. Price, $2. Pp. 261, with illustrations. New York & London: Whittlesey House, McGraw-Hill Book Company, Inc., 1940.

Professor Pitkin has been author, dean and teacher and has previously written books on the art of rapid reading and on the art of learning. He recommends that the way to learn to write usefully is first to learn to write much. He recommends particularly study of condensation. In his own practice he learned eventually to write 1,500 words an hour and he now claims that he can write 10,000 words in finished book copy in nine consecutive hours. He recommends also that every writer plan to organize his information in useful files. His book is full of useful information but whether or not it is possible by the use of a book of this kind to become a writer one can only say that Mr. Pitkin says that it is. He provides innumerable exercises and plans for study. No doubt any one who has a talent and an urge for writing will be helped by this book. As an old practitioner in the writing field, the reveiwer is inclined to believe that without this urge and talent any amount of sweat and exercise will not produce writing that is useful or salable.

Die Entzündungsbestrahlung. Von Dr. med. habil. R. Glauner, Dozent für Röntgenologie an der Universität Köln. Boards. Price, 15 marks. Pp. 190, with 14 illustrations. Leipzig: Georg Thieme, 1940.

Illustrative of the enlarging field for application of roentgen therapy other than in the treatment of cancer, this book is a welcome addition to the literature, constituting an excellent summary of the known technical and clinical facts relative to the subject. After a brief historical introduction and a discussion of the concept of inflammation, the author proceeds to the full consideration of the effect of the roentgen rays on local inflammatory processes from the standpoint of the physical and chemical changes, the blood vessels, the exudates, the mesenchyma and ferments. Next comes the discussion of the influence of the roentgen rays on the exciting causes of inflammation and on the general defensive mechanism of the organism against inflammation, including the antibactericidal blood and serum reactions, the reticulo-endothelial systems, the action of the protein bodies, the blood picture and the vegetative nervous system. The clinical subsidence of experimental inflammation under roentgen irradiation is next studied from the standpoint of bacterial, mechanical and chemical inflammation. Then the author proceeds to a general clinical consideration of anti-inflammatory irradiation, giving the indications and contraindications, general technic and dosage. The second part of the book is devoted to a discussion of radiation therapy in inflammations by systems, including a long list of inflammatory lesions in which the value of roentgen therapy is but slightly appreciated by the majority of the medical profession. This book, which is gotten up in such an authoritative manner, should serve to stimulate a much wider use of roentgen therapy in the treatment of inflammations.

Three Famous Occultists. Dr. John Dee. By G. M. Hort. Franz Anton Mesmer. By R. B. Ince. Thomas Lake Harris. By W. P. Swainson. Cloth. Price, $2. Pp. 190. Philadelphia: David McKay Company, [n. d.].

In the sixteenth century John Dee practiced as an astrologer. In those days the drawing of horoscopes was considered a science. Dee actually drew horoscopes for Queen Mary and for her sister Princess Elizabeth. Among other contributions he wrote a work on naval defense. Early in his career he became interested in psychic manifestations, recording his dreams and other phenomena. He also is credited with having practiced crystal gazing and the original crystal is still available in the British Museum.

Franz Anton Mesmer has been the subject of many biographies. He was the originator of magnetic healing, constantly in debate with the medical faculty of his time. In 1784 a commission was appointed to investigate the claims of animal magnetism and published a report which refuted his claims. At that time the scientific study of suggestion was not yet known. A description of his technic indicates that the results were secured by the power of suggestion, which was enhanced by the laying on of hands and by some complicated apparatus.

The third of the occultists, Thomas Lake Harris, was an Englishman who came early to America. In 1844 he was a Universalist preacher in New York. He became an occultist in 1850, when he first experienced what he termed "internal respiration." As was customary in those days, he formed a community to be called the Brotherhood of the New Life, which practiced occultism in a form which was apparently a mixture of astrology, alchemy and other esoteric manifestations. He had a system of religious philosophy based on christianity, and he claimed to have overcome death. When he himself died, many of his followers lost interest.

Government and Economic Life: Development and Current Issues of American Public Policy. Volume II. By Leverett S. Lyon and Victor Abramson. With the collaboration of Charles L. Dearing, et al. The Institute of Economics of The Brookings Institution Publication No. 83. Cloth. Price, $3.50. Pp. 1,301. Washington, D. C.: Brookings Institution, 1940.

This is the second volume of a series on American public policy in relationship to economic life prepared through the Brookings Institution and published by it. In this volume the major portion of the discussion concerns government and the special treatment of private enterprise. One chapter deals with the activities of the government in the field of foods and drugs. There are also chapters on public relief and on social security. In their concluding observations the authors incline to the view that "our economy has reached a stage which is denominated as 'mature' and that as a result there is no longer any hope that we shall be able to come near the full employment of our productive resources without a continuous program of extensive public spending designed specifically to promote the utilization of idle men and plant." They recognize that it has not been demonstrated by economic analysis or by practice that the means now in operation for meeting the problem of unemployment will do more to meet the situation than the less elaborate programs of the early thirties. They say, however, that a permanent program of extensive governmental spending raised great questions of effectiveness and perhaps the survival of private enterprise.

A Surgeon Explains to the Layman. By M. Benmosché, M.D. Cloth. Price, $3. Pp. 317, with diagrams by Bhola D. Panth. New York: Simon & Schuster, 1940.

While there are innumerable works of medicine planned primarily for the public, no one has previously attempted to inform the lay reader concerning all the technical details and background of surgical procedures. To this extent Dr. Benmosché is a pioneer. The information is for the most part sound and readable. He does not attempt to cover the history of surgery as in Graham's excellent book "The Story of Surgery." If any one wants to know about his operation before he has it, there is probably no better guide. However, from the point of view of the patient there may be some question as to the desira-

bility of a work of this character. In every instance the reader is made to feel that the decision of when to operate or whether or not to operate at all is an exceedingly difficult one. Incidentally it is a task which the surgeons find sufficiently difficult without having to enter into debate with the uninformed patient. Of chief value in the work are the simple discussions of the anatomy of various portions of the body. Particularly impressive are the final discussions of surgery of the chest, the brain and the heart. Quite recently the picture periodicals have illustrated every step of several surgical operations and there has been at least one broadcast directly from an operating room. Thus a beginning has been made. It will be interesting to observe the ultimate effect of information for the public concerning the technical details of operative procedures.

Electric Light for the Farmstead. Prepared by Bureaus of Agricultural Chemistry and Engineering and Home Economics. U. S. Department of Agriculture, Farmers' Bulletin No. 1838. Paper. Price, 10 cents. Pp. 61, with 43 illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1940.

This bulletin stresses the importance of good lighting and discusses in detail the essentials for good lighting. Further, it describes methods for providing good light for the farmhouse. The types of electric outlets, remodeling old lighting installations and equipment as well as lighting the farm yard and lighting the farm buildings are discussed. Information on planning lighting for farm buildings is given and is based on observations and records of the Department of Agriculture.

Pharmacology and Therapeutics. By Arthur R. Cushny, M.A., M.D., LL.D. Twelfth edition revised by C. W. Edmunds, A.B., M.D., Professor of Materia Medica and Therapeutics in the University of Michigan, Ann Arbor, and J. A. Gunn, M.A., M.D., D.Sc., Professor of Pharmacology and Director of the Nuffield Institute for Medical Research, University of Oxford, Oxford. Cloth. Price, $6.50. Pp. 852, with 66 illustrations. Philadelphia: Lea & Febiger, 1940.

Since its first appearance in 1899 this work has been enjoying increasing popularity in Great Britain and the United States as a standard textbook and as a reference book on the subject of pharmacology by teachers, students and practitioners. Considerable revision has been made in the twelfth edition, beginning with the title, which was formerly "A Text-Book of Pharmacology and Therapeutics, or the Action of Drugs in Health and Disease" but now bears the simplified wording "Pharmacology and Therapeutics," extending through the introduction, the subject material and the index. Some of the changes are minor in nature but many involve considerable revision and even the addition of subjects formerly foreign to this book. Hardly a section has escaped some revision, but included in the sections which have undergone major changes, rewriting or additions are those describing the heavy metals and metalloids, alcohol-chloroform group, soporifics or hypnotics, local anesthetics, nicotine group, drugs of internal secretion and the vitamins. Several totally new descriptions have been inserted, including pharmacologic syndromes in the introduction, benzedrine, sex hormones, sulfanilamide, sulfapyridine and allied compounds and mandelic acid. These additions account for most of the increase in size of forty-four pages.

The section on the opium series remains as excellent as ever and includes a new member, bulbocapnine, an alkaloid closely related to apomorphine. One of the most useful and unique features in Cushny's Pharmacology and Therapeutics has been the classification of drugs according to their therapeutic uses. The student has always appreciated this section.

It is difficult to prepare a textbook on pharmacology for two countries such as Great Britain and the United States of America, as there is considerable difference in the nomenclature. For example, butyl-bromallyl barbituric acid is known as pernocton in England and this is the name which appears in the text. In the United States the preparation is known as pernoston. Another example is seen under the section on avertin. In the British market avertin is supplied as avertin fluid but on the American market it is supplied as avertin with amylene hydrate, the amylene hydrate possessing anesthetic properties almost equal to those of avertin. However, even with such differences the subject material is so clearly and interestingly written that even the student will encounter few difficulties in his reading.

Although the index has been enlarged, it still appears to be too conservative for a book which contains so much information. Unfortunately, the publishers have changed the color of the cover from the former familiar green to a red which is not unlike the covers of other well known books on pharmacology. No longer can one go to the library and easily pick out this book by its distinctive color. However, it will still remain one of the most popular works on pharmacology.

A Manual of the Common Contagious Diseases. By Philip Moen Stimson, A.B., M.D., Assistant Professor of Clinical Pediatrics, Cornell University Medical College, New York. Third edition. Fabrikoid. Price, $4. Pp. 465, with 60 illustrations. Philadelphia: Lea & Febiger, 1940.

Complete revision of a previously excellent textbook on the contagious diseases has produced here a book of great value. The subjects discussed include the principles of contagion, serum reactions, detailed description of the common contagious diseases, general management of these disorders, and management in boarding schools and homes. The material is presented briefly and the appended references increase the value of the work. Included is a discussion of the use of sulfanilamide and sulfapyridine. The book covers practically every phase of the subject without wordiness, so that physicians, students and nurses will find satisfaction in having this volume at their disposal.

Behind the Surgeon's Mask. By James Harpole, pseud. Cloth. Price, $2.75. Pp. 308. New York: Frederick A. Stokes Company, 1940.

Here is another collection of interesting anecdotes from the practice of medicine by a British writer who has exceptional qualities in the field of letters. He has, moreover, an excellent sense of the dramatic and is able to make fascinating the incidents which many another physician might pass as commonplace. Both doctors and layman will find this book interesting. Moreover, it has none of the aspects of horror or tribulation which make many such works forbidden for the invalid.

A Survey of the Hospital Dietitian and Her Job. Parts I and II. By S. Margaret Gillam, Department of Nutrition, The New York Hospital, New York. Reprinted from Journal of the American Dietetic Association Vol. XVI: Nos. 6 and 7, 1940. Paper. Pp. 41. Chicago, 1940.

This is a report of a study of the hospital dietitian and her functions, activities and professional relationships. It is based principally on the questionnaire method.

Aids to Inorganic Chemistry. By R. G. Austin, B.Sc., A.I.C., F.R.M.S., Associate of University College, Southampton. Cloth. Price, $1.50. Pp. 348. Baltimore: William Wood & Company, 1940.

This brief handbook provides the fundamental information regarding inorganic chemical substances that is necessary to all students in elementary courses on chemistry. The book should be especially valuable as an aid in preparation for examination.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Foot Drop Following Operation on the Knee; Res Ipsa Loquitur.—The plaintiff ruptured the exterior lateral and posterior crucial ligaments of his left knee and engaged the defendants to repair the damage. An operation was performed consisting of the removal of the damaged portions of the ligaments and the substitution of new material obtained from the fascia lata and biceps femoris muscle of the left leg. After the operation, the plaintiff began to suffer from a foot drop, and an examination by physicians other than the defendants disclosed that the peroneal nerve, the nerve supply to the muscles which raise the foot, was severed in the vicinity of the knee. The plaintiff then sued the defendants, alleging negligence, and judgments for the defendants resulted. After the case had been considered by the district court of appeal, California (80 P. (2d) 96; abstr. *J. A. M. A.* **112:**1419 [April 8] 1939), the plaintiff appealed to the Supreme Court of California.

The medical testimony in this case, said the Supreme Court, showed without contradiction that, although the severance of the peroneal nerve is something which ordinarily does not occur in operations such as that performed in this case, yet even

when the precautions prescribed by the approved technic are taken, there may be a break of or an injury to the nerve in from 5 to 9 per cent of the cases. The court could find nothing startling about such evidence and was of the opinion that it afforded no basis for the recovery of damages. Probably in any operation, the court observed, there is some hazard which the medical profession recognizes and guards against but which is not always overcome. To say that the doctrine of res ipsa loquitur permits the recovery of damages in every case where an injury does not ordinarily occur would place a burden on the medical profession which the law has not heretofore laid on it. On the contrary, the law has never held a physician or surgeon liable for every untoward result which may occur in medical practice. It requires only that the physician shall have the degree of learning and skill ordinarily possessed by physicians of good standing practicing in the same locality and that he shall use ordinary care and diligence in applying that learning and skill to the treatment of his patients. Whether he has done so in a particular case is a question for experts and can be established only by their testimony. When the matter in issue is one within the knowledge of experts only and is not within the common knowledge of laymen, the expert evidence is conclusive. Negligence on the part of a physician will not be presumed; it must be affirmatively proved. In the absence of expert testimony it will be presumed that a physician exercised the ordinary care and skill required of him in treating his patient.

It is true, the court continued, that in a restricted class of cases the courts have applied the doctrine of res ipsa loquitur in malpractice cases. But it has been invoked only where a layman is able to say as a matter of common knowledge and observation that the consequences of professional treatment were not such as ordinarily would have followed if due care had been exercised. For example, it has been applied in California where a sponge was left in the body of the patient, where the patient was burned by the application of hot compresses or heating apparatus or through the operation of an x-ray machine and where the patient sustained an infection through the use of an unsterilized hypodermic needle. In each of these situations, however, the rule was applied because, in the opinion of the court, common knowledge and experience teaches that the result was one which would not have occurred if due care had been exercised. In the present case, however, an entirely different situation existed. Here what was done lies outside the realm of a layman's experience. Medical evidence is required to show not only what occurred but how and why it occurred. That evidence in the present case established beyond question, the court thought, not only that the peroneal nerve may be injured even when due care is used but that this unfortunate result invariably occurs in a limited number of cases. The doctrine of res ipsa loquitur is therefore entirely inapplicable and no malpractice was proved. The court, therefore, affirmed the judgments for the defendants.—*Engelking v. Carlson (Calif.), 88 P. (2d) 695.*

Optometry: Sale of Eyeglasses by Optometrist Subject to Retail Sales Tax.—In two decisions, one emanating from Pennsylvania and the other from California, the question of the applicability of a retail sales tax to sales of eyeglasses by optometrists was decided. In each case the optometrist, after testing his patient's eyes and prescribing glasses therefor, sent the prescription to a dispensing optician, received the glasses therefrom and then delivered them to the patient. The bill that the optometrist subsequently sent to the patient included a fee for his professional services and a profit from the sale of the eyeglasses.

In *Kamp* v. *Johnson,* the plaintiff, an optometrist, sued the treasurer of the state of California to recover the amount of a tax which the optometrist had paid under protest. He contended that he was not subject to the provisions of the California Retail Sales Tax Act of 1933 because he was engaged in the practice of a profession and the furnishing of eyeglasses was purely incidental to the rendering of professional services. From an adverse judgment the optometrist appealed to the Supreme Court of California. In affirming that judgment, the Supreme Court held that the fact that the plaintiff practiced a profession was immaterial because all the elements determinative of liability under the Retail Sales Act were present, i. e., a retail sale of tangible personal property for use by the patient and not a sale for resale, a transfer of title to the patient and the payment of a consideration therefor. In the judgment of the court the tax properly fell on the optometrist, since "the tax must be paid at some time with respect to all tangible personal property sold for use or consumption."

In *Commonwealth* v. *Miller,* the state of Pennsylvania sued the defendant optometrist to collect a tax assessed under the Pennsylvania Mercantile License Tax Act of 1899. It was conceded that the defendant was not liable for payment of the tax with respect to any income derived from his professional services in examining and measuring the vision of the eyes, prescribing glasses and fitting them after they were made. The defendant contended, however, that he should be declared exempt from the tax as to the selling of eyeglasses because an optometrist in selling glasses is in the same position as a dentist selling bridgework or a physician supplying medicine to his patients. From an adverse judgment the optometrist appealed to the Supreme Court of Pennsylvania. The making and selling of bridgework by a dentist, said the Supreme Court, and the supplying of medicine to patients by a physician, instances in which the state "has very correctly not attempted to collect the mercantile tax," are radically different from the selling of eyeglasses by optometrists. In the case of the dentist, said the court, the preparation of bridgework necessitates considerable professional and scientific skill, labor and design on the part of the dentist. In the case of the physician, it is quite obvious that the furnishing of medicine to a patient is an inherent part of a physician's professional services in the treatment of sickness and disease. But the optometrist in selling eyeglasses is engaged in a business not at all necessary to his profession. He does not grind the lenses nor place them in their fittings. He plays no part in making or creating the eyeglasses. The glasses are handed to him by the maker, the optician, and he makes any necessary adjustment to fit them to the patient's head, but in so doing he makes no real change in the lenses or frames as such. No skill, scientific or otherwise, of the optometrist is required, since the scientific work has already been performed by the optician in making the glasses. In the judgment of the court the sale of eyeglasses, tangible chattel, is readily separable from the essential professional service of the optometrist, and such sale properly belongs to the occupation of the optician and is not necessary to the practice of optometry. The retail optician has always been subject to the mercantile tax and the optometrist cannot invade the optician's field of business, be a vendor of merchandise, and then claim immunity from the tax merely because he is also engaged in the profession of optometry. The court held, therefore, that the defendant was subject to the tax, and so it affirmed the judgment in favor of the state.—*Kamp v. Johnson (Calif.), 99 P. (2d) 274; Commonwealth v. Miller (Penna.), 11 A. (2d) 141.*

Society Proceedings

COMING MEETINGS

American Orthopsychiatric Association, New York, Feb. 20-22. Dr. Norvelle C. La Mar, 149 East 73d Street, New York, Secretary.

Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, Feb. 17-18. Dr. W. D. Cutter, 535 North Dearborn St., Chicago, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 27. Dr. Walter H. Theobald, 307 North Michigan Blvd., Chicago, Chairman.

Pacific Coast Surgical Association, Los Angeles, Feb. 19-22. Dr. H. Glenn Bell, University of California Hospital, San Francisco, Secretary.

Southern Section, American Laryngological, Rhinological and Otological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, San Francisco, Feb. 1-2. Dr. Robert C. Martin, 384 Post St., San Francisco, Chairman.

Society of Surgeons of New Jersey, Newark, Jan. 29. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

200:577-716 (Nov.) 1940

*Pulmonary Embolism and Heart Disease: Review of Twenty Years of Personal Experience. P. D. White, Boston.—p. 577.
Cobra Venom: Its Use in Stenocardia: Preliminary Report. A. E. Parsonnet and A. Bernstein, Newark, N. J.—p. 581.
Heredity in Pernicious Anemia. H. F. Stamos, Ann Arbor, Mich.—p. 586.
Effect of Nicotinic Acid on Blood Coagulation. R. M. Calder and Grace P. Kerby, Houston, Texas.—p. 590.
Culture of Human Marrow: Studies of Relative Effectiveness of Neoarsphenamine, Mapharsen, Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfamethylthiazole on Infections with Streptococcus Viridans (Alpha Hemolytic Streptococcus). E. E. Osgood, with technical assistance of Inez E. Brownlee and Julia Joski, Portland, Ore.—p. 596.
Quick's Prothrombin Test Simplified by Use of Stable Thromboplastin. A. W. Souter and R. Kark, Boston.—p. 603.
*Mechanism of Renal Hypertension. J. M. Muñoz, E. Braun-Menendez, J. C. Fasciolo and L. F. Leloir, Buenos Aires, Argentina.—p. 608.
*Clinical Experience with Sulfamethylthiazole. A. E. Brown and W. E. Herrell, Rochester, Minn.—p. 618.
Antipyretic Action of Sulfapyridine. P. B. Beeson and C. A. Janeway, Boston.—p. 632.
Intubation Studies of Human Small Intestine: XV. Absorption and Expulsion of Glucose from Stomach. R. Warren, W. G. Karr, Olive D. Hoffman and W. O. Abbott, Philadelphia.—p. 639.
Sabin Agglutination Test and Polysaccharide Skin Test (Francis) as Indexes of Recovery in Pneumonia. W. W. Fox, R. Rosi and W. L. Winters, Chicago.—p. 649.
Diagnosis of Cause of Obstructive Jaundice by Means of Blood Picture. T. R. Waugh, Montreal.—p. 655.
Relation of Phosphorus to Fat and Glucose Metabolism in Sprue. F. M. Hanes and R. Reiser, Durham, N. C.—p. 661.
Central Nervous System Stimulant Effects of Dextro-Amphetamine Sulfate. M. Prinzmetal, Los Angeles, and G. A. Alles, San Francisco.—p. 665.
Influenzal Meningitis Treated with Sulfapyridine: Bilateral Ureteral Obstruction, Uremia, Recovery. J. H. Arnett, G. D. Shoup and N. W. Henry, Philadelphia.—p. 674.
Delirium Tremens: Study of Various Methods of Treatment. M. Rosenbaum, P. Piker and H. Lederer, Cincinnati.—p. 677.
Production of Fatty and Fibrotic Livers in Guinea Pigs and Rabbits by Seemingly Adequate Diets. M. A. Spellberg and R. W. Keeton, Chicago.—p. 688.
*Endemic Riboflavin Deficiency in Infants and Children. T. D. Spies, W. B. Bean, R. W. Vilter, Cincinnati, and N. E. Huff, Birmingham, Ala.—p. 697.

Pulmonary Embolism and Heart Disease.—White summarizes his experience of twenty years with pulmonary embolism in association with heart disease by recounting the increasing frequency with which he has recognized the condition, the possible confusion in diagnosis, the frequency with which it complicates heart disease and the helpful signs of its presence. From 1920 to 1930 among 4,000 patients he made an initial definite diagnosis of pulmonary embolism simulating or complicating heart disease in only 9 cases and a questionable diagnosis in only 7. Among 3,350 patients in the last decade the definite diagnoses have increased from 9 to 66 and the questionable ones from 7 to 39. Of the 75 definite cases only 29 were diagnosed in the first sixteen of the twenty years, while 46 cases were encountered among 1,350 patients in the last four years. The author is certain that this increase in the last few years has not been actual but that a large part of it has been due to better recognition of the condition. Twenty-eight of the 75 definite cases simulated and 47 complicated heart disease. The cardiac diagnoses in which pulmonary embolism or infarction occurred as a complication were coronary disease, mostly with myocardial infarction and with or without hypertension, in 26; rheumatic heart disease, mostly with mitral stenosis and auricular fibrillation, in 15; hypertensive heart disease in 2, patent ductus arteriosus with subacute bacterial endocarditis in 1 and cardiac enlargement with no other evident abnormality than chronic auricular fibrillation or flutter in 3. Peripheral phlebitis was evident in only a few cases, but it is probable that the majority might have shown such a lesion if the veins could have been explored; at least that is the lesson to be derived from the postmortem observations in which phlebitis that gives little or no clinical evidence of its presence is found in 70 per cent of cases of medical pulmonary embolism. Pulmonary embolism has failed to attract the interest and attention it has deserved from general practitioners as an important medical disease in nonsurgical and nonobstetric cases. Usually pulmonary embolism is either so mild or so rapidly fatal that characteristic electrocardiographic abnormalities are not present or the patients are examined only after the height of the effect of the pulmonary arterial obstruction has passed. Pulmonary embolism and infarction are easily overlooked, especially in the presence of congestive heart failure, when they are most common; or they are erroneously diagnosed as pneumonia, congestive heart failure or coronary thrombosis. Clues to the diagnosis lie in unexplained fever, leukocytosis, tachycardia, faintness, prostration, dyspnea or even jaundice, especially in a patient with heart disease.

Mechanism of Renal Hypertension.—Muñoz and his associates epitomize the present knowledge of the mechanism of renal hypertension as follows: Renal ischemia determines the secretion of "renin," which is an enzyme and acts on a blood globulin ("hypertensin precursor") and gives rise to a substance ("hypertensin") which produces vasoconstriction. Another enzyme, "hypertensinase," which destroys hypertensin, is present in blood and body tissues. A better understanding of the mechanism of renal hypertension may suggest the treatment of this disease which should aim at suppressing or diminishing the secretion of renin by the kidney, inhibiting the reaction of renin with blood globulin, diminishing the amount of hypertensin precursor and inhibiting the action of hypertensin by increasing the amount or the activity of hypertensinase or some other neutralizing agent. After injection of renin into chloraloosed dogs, the hypertensin precursor decreases and even disappears from their blood. After nephrectomy, the hypertensin precursor increases and hypertensinase decreases.

Clinical Experience with Sulfamethylthiazole.—Brown and Herrell review their clinical experience with the use of sulfamethylthiazole in 30 cases of pneumonia, 7 of septicemia, 5 of acute bacterial endocarditis, 5 pelvic infections, 4 osseous infections, 25 cutaneous infections, 13 infections of the ear, nose and throat, 3 urinary infections and 14 cases of miscellaneous infections; a total of 106 cases. The drug was administered orally to the majority of the patients in doses similar to sulfanilamide and sulfapyridine. However, larger doses were frequently used for and tolerated by the severely ill patients. The sodium salt of sulfamethylthiazole was used intravenously for 3 patients and it significantly elevated the concentration of the drug in the blood. Sulfamethylthiazole orally produced concentrations of the free drug in the blood similar to but somewhat lower than those that result from sulfapyridine. A minimal amount of conjugation occurred with sulfamethylthiazole. The results obtained to date from its use seem to substantiate experimental predictions. Staphylococcus aureus and Diplococcus pneumoniae (type I) infections in particular seem to respond to treatment. With the exception of lower motor neuron involvement in 3 cases and of cutaneous eruptions in 9, toxic effects seemed to be less than those encountered following the use of sulfapyridine and sulfanilamide. Significant nausea and emesis occurred infrequently. The danger of lower motor neuron involvement makes it unwise to use sulfamethylthiazole for mild infections caused by Staphylococcus aureus. However, a fulminating infection which carries a high mortality rate far outweighs the danger of toxic manifestations from drug therapy, and this drug or a related preparation may be indicated.

Endemic Riboflavin Deficiency in Children.—During a period of two years Spies and his colleagues examined repeatedly 472 children, from 5 months to 14 years of age, of parents with deficiency diseases. They paid particular attention to their physical and mental development and to the presence or absence of lesions of riboflavin deficiency. They made a clinical diagnosis if one or more of the deficiency lesions ("chei-

losis," the reddened macerated areas at the angles of the mouth and the linear lesions or fissures of the lips and the ocular symptoms characterized by bulbar conjunctivitis, lacrimation, burning of the eyes and failing vision) were present. Cheilosis was observed in 113 cases, linear lesions in 93 and ocular manifestations in 167. These children were usually underweight and underdeveloped for their age. Many were apathetic and indifferent and made poor progress in school. Frequently they complained of sore mouths and burning and itching eyes. The symptoms waxed and waned with the seasons and with changes in the quality of the dietary, but they appeared most frequently during the spring and summer. Increased exercise and infections seemed to precipitate the appearance of lesions in borderline cases. The response of the children to synthetic riboflavin or substances rich in it was gratifying. The cheilosis healed rapidly, the ocular symptoms disappeared and their general health improved. Unless therapy was continued or the diet improved, the disease tended to recur. Dietary studies showed that almost without exception the mothers of these children had subsisted on grossly inadequate diets during pregnancy and lactation, and also that the majority of the infants and children studied received only 35 per cent of the estimated requirement of riboflavin. The average case responded satisfactorily to the oral administration of 1 mg. of riboflavin three times a day, 1 ounce of brewers' yeast or liver extract daily.

American Journal of Orthopsychiatry, Menasha, Wis.

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*Roentgen Treatment of Adrenal Glands in Angina Pectoris, 100 Cases. W. Raab, Burlington, Vt.—p. 688.
Specialization in Internal Medicine. W. B. Breed, Boston.—p. 711.

Tetanus Toxoid Immunization in the Navy.—Hall summarizes the work on active immunization against tetanus which began in 1934 on the fleet hospital of the United States Navy, the U. S. S. *Relief*. Since then 3,446 midshipmen of the Naval Academy as well as other navy personnel and dependents have been immunized. The freedom from reactions in the use of alum precipitated toxoid has been universally noted. Soreness of the arm, disappearing in forty-eight hours or sooner, occurred from injections given intramuscularly. When injections were made subcutaneously a cutaneous reaction occurred which was greater in intensity the closer to the skin the material was placed. This was followed by a subcutaneous induration which remained as a nodule for one or two weeks. The intramuscular route was chosen because of its relative freedom from local reaction. It has been suggested that immunity is enhanced when the material is placed in the skin. This has not been the observation in the Navy, as no uniformly higher level of antitoxin titer was observed in those who had a violent cutaneous reaction than in those in whom the injection was made intramuscularly and who had little or no cutaneous reaction. General reaction has been minor, seldom amounting to more than mild malaise and an occasional minor and short rise in temperature. Some reactions were encountered when a certain toxoid was used. The reactions were probably caused by inadequate washing of the alum precipitated toxoid in the course of preparation. No case of tetanus among the immunized individuals has as yet been reported. The actual antitoxin level in the blood is not of prime importance. Basic immunity, or the ability of tissue to react with the production of antitoxin, is the essential condition. The plan adopted in the Navy is to give two injections eight weeks apart as basic immunization, injection at the time of injury, if deemed necessary to raise blood antitoxin rapidly, and injection every four years after basic immunization to maintain immunity at a high level. All midshipmen at the U. S. Naval Academy are now immunized with alum precipitated tetanus toxoid. Such immunization is ideally fitted to the needs of the military services and to other groups which can be well controlled. Its universal adoption in such groups seems inevitable.

Prevention of Pernicious Anemia.—Askey believes that the challenge for the future must be to diagnose pernicious anemia before blood and nervous system changes appear. He presents the accumulating evidence that potential cases are to be looked for in the relatives of patients and suggests a scheme by which they may be recognized in the latent stage. Pernicious anemia has been found in several members of families to an extent far above the expectation from chance alone. Increased frequency of pernicious anemia among relatives should be reflected in an increased incidence of its precursor, anacidity. All the studies of relatives analyzed as to age and the nearness of blood relationship show an increased incidence of anacidity, particularly in the two decades prior to 40, and about a double percentage of anacidity among the near relatives as opposed to distant relatives. Of a total of 174 cases in which previous gastric analyses had been recorded, 171 showed anacidity. Except in rare cases, true anacidity is found in pernicious anemia and must necessarily precede its development. Those relatives with a pernicious anemia genotype should show histamine refractory anacidity for a variable period prior to the manifestation of the anemia. Such a finding justifies at least the suspicion of potential pernicious anemia. The presence of free acid indicates that the risk of the immediate development of the anemia is small. During the last six years the author adopted a tentative scheme for the study of families in which pernicious anemia was present. He arbitrarily accepted heredity as the most important etiologic factor and considered the family as the unit of greatest potential concentration. Ten families were discovered with two or more persons having the disease, and 10 were collected from fellow internists in Los Angeles. In 18 of these 20 families the familial occurrence was proved; in 2 it was based on hearsay. Every patient was told of the familial nature of the disease and requested to have his relatives come in for a histamine gastric analysis. Many relatives refused, but 61 agreed and 10 of these showed anacidity. In the families thus studied, severe crippling pernicious anemia has since developed in 2 relatives who refused to have gastric analyses. Of the 10 anacid relatives, signs or symptoms of early pernicious anemia have developed in 4, hypochromic anemia (apparently idiopathic) in 2, 3 have normal blood and 1 cannot be located. Of the 4 cases believed to be incipient pernicious anemia, 3 were proved to be macrocytic. In 1 the diagnosis was thought justifiable owing to clearcut history of glossitis and paresthesias relieved by liver. The development of hypochromic anemia in 2 cases stresses the tendency of the apparently idiopathic form to appear in pernicious anemia families. Whether there is latent or coexistent

pernicious anemia can only be conjectured. Achlorhydria suggests the importance of knowing whether the patient has or has had a familial history of pernicious anemia. Since pernicious anemia may occur only in a single generation, it would seem important that the patients with achlorhydria be advised of this hereditary tendency so that their grandchildren may be able to make a positive statement regarding its familial occurrence. The physician should study the family rather than the patient alone. The anacid relatives should be watched for early signs and symptoms. It appears unwise to acquaint them with the early symptoms, as it would lead to the promiscuous use of liver and prevent the recognition of the early development. The insidious development of severe spinal cord damage may be prevented in many cases if the relatives of pernicious anemia patients are sought out and grouped by means of the histamine gastric analysis.

Four-Meal Diet for Diabetes Mellitus.—Margolis and Eisenstein point out that, despite technical refinements and improvements in the uniformity and stability of the new insulins, culminating in protamine zinc insulin, frequent failings of their slower actions have become apparent. Their failings are manifest in diurnal glycosuria, in the necessity for supplementary injections of regular insulin, in serious, even fatal, reactions and often in the abandonment of protamine zinc insulin in many cases in which its aid would have been most welcome. The authors were able to circumvent the obstacles by providing optimal dextrose absorption in relation to the action of protamine zinc insulin. Since the maximal depression of the blood sugar level occurs from ten to twenty-four hours after the injection of protamine zinc insulin, an adequate supply of carbohydrate was made available at the time of its greatest need by giving a liberal carbohydrate meal late in the evening, furnishing carbohydrate which is fed into the blood stream during the night slowly and continuously. This four-meal procedure yielded smooth and relatively rapid diabetic control, even in severe cases, and has in their experience successfully averted the most disagreeable features encountered when protamine zinc insulin is used. Diurnal glycosuria was apparently more readily controlled, nocturnal reactions were avoided, the need for supplementary regular insulin was obviated and the simplicity of management with protamine zinc insulin alone, that is a single daily injection, was gained. The records of 14 representative diabetic patients of various ages and with different degrees of illness are cited by the authors in the hope of stimulating a more intensive trial by others. They state that, since a single injection of protamine zinc insulin cannot be placed precisely at points around the clock where food is, the food can be placed, with a high degree of safety, where the greatest insulin action is.

Roentgen Treatment of Adrenals in Angina Pectoris.—Raab advances the theory that attacks of stenocardiac pain on effort, psychic emotion or cold are caused by anoxia of the cardiac muscle. This is largely due to acute discharges of epinephrine from the adrenals occurring physiologically under these conditions. Epinephrine exerts a specific anoxiating effect on the cardiac muscle which under normal circumstances is compensated by simultaneous dilatation of the coronary arteries. This compensatory mechanism must fail when the coronary arteries are unable to dilate adequately because of coronary sclerosis and thus an abnormally exaggerated painful degree of myocardial asphyxia results. Attempts to relieve the symptoms of angina pectoris by restricting the acute discharges of epinephrine through roentgen irradiation of the adrenals were successful in 76 of 100 patients. These patients had typical attacks of angina pectoris on effort, emotion or cold; several of the cases were of the severest kind. Sixty-two patients were entirely or almost entirely freed from complaints or, at least, considerably improved for an average of thirteen and one half months, 14 patients were moderately improved for an average of seven and one half months and 24 patients did not respond. Electrocardiographic signs of myocardial anoxia disappeared partly or completely in most of the successfully treated patients but remained unchanged in those whose complaints were not improved. The blood pressure, either high or normal, remained practically unchanged in all instances.

Archives of Neurology and Psychiatry, Chicago

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*Hereditary Primary Glaucoma: Pedigree with Five Generations. W. H. Stokes, Omaha.—p. 885.
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Anticataractogenic Action of Certain Nitrogenous Factors. Helen S. Mitchell, Gladys M. Cook and Mary D. Henderson, Amherst, Mass.—p. 990.
Ocular Conditions Associated with Clinical Riboflavin Deficiency. L. V. Johnson and R. E. Eckardt, Cleveland.—p. 1001.

Hereditary Primary Glaucoma.—Stokes reports the occurrence of glaucoma in five generations. The history is as follows: William S., born in 1799, became totally blind fourteen years before his death at the age of 47. Of his two children Joe, who had normal eyes, did not marry; but Elizabeth became blind gradually while still young and for several years before death at the age of 46 she suffered from severe "neuralgic" pains in her head (absolute glaucoma). Five of her 8 children became totally blind in their early twenties. One of these, a woman of 84, is still living. The 4 children of one of these 5 affected patients are not in sympathy with the medical profession and neither they nor their children are available for examination, but of the other 4 patients having 18 children 7 were affected; 4 other children died early (at 14, 9, 6 and 2 years respectively) of typhoid. The children and the grandchildren of the 3 youngest persons of this sibship, the third generation, who did not have glaucoma did not acquire the disease. The fourth generation glaucoma came on during the second, third and fourth decades. Five of the 7 affected persons of the fourth generation married and they had 24 children, of whom 7 had glaucoma

between the ages of 15 and 31. The 6 children of the sixth generation, from 1 to 8 years of age, have been examined when their eyes were apparently normal, but they are as yet too young to have acquired the disease. The author states that hereditary glaucoma appears to result from a simple dominant and not from a sex-linked gene, as the transmission by the two sexes in the foregoing pedigree was equal. As far as he can judge from this pedigree, the chance that an offspring of a glaucomatous person would be similarly affected is about 50:50 and the chance of an offspring of a normal person appears negligible. Consanguinity did not occur in this pedigree. The reduced age of onset in the younger generation must not be taken as proof of a general tendency to anticipation of the disease. Hereditary glaucoma usually, but by no means always, appears in a chronic form. It is possible that a local or general disposition to glaucoma is inherited and the appearance of the disease depends on other factors, either inherited or acquired. The incidence of myopia was sufficiently great to suggest that the hypertension had been influential in producing refractive abnormality. There is no evidence that a beneficial outcome will result without operation. The only permanently good results were obtained in persons having one of the fistulizing operations. The best results were obtained when the operation was performed when glaucoma was still in the compensatory stage; that is, before irreversible secondary anatomic and pathologic changes occurred.

Archives of Physical Therapy, Chicago

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Physical Therapy and Bronchoscopy. J. D. Kernan, New York.—p. 620.

Canadian Medical Association Journal, Montreal

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*Hypertension in Girl of 12, Associated with Unilateral, Chronic, Atrophic Pyelonephritis, Treated by Nephrectomy. F. S. Patch, L. J. Rhea and J. T. Codnere, Montreal.—p. 419.
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*Id.: II. Tests with Gentian Violet in Treatment of Pinworm Infection. M. J. Miller, L. Choquette, W. Audet, R. F. Kelso and J. A. Guenette, St. Anne de Bellevue, Que.—p. 455.
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Cancer of Rectum. J. A. MacFarlane, Toronto.—p. 467.
*Fatal Serum Reaction: Case. R. Ferguson, Montreal.—p. 469.

Hypertension in Young Girl Associated with Pyelonephritis.—Patch and his colleagues report a case of hypertension in a girl of 12, who was found to have a unilateral atrophic pyelonephritis and who has been apparently cured by nephrectomy. At the age of 18 months she had an illness lasting a few days for which a diagnosis of pyelitis was made. Since then she has had intermittent illnesses with nausea, epigastric pain and malaise. Cystoscopy was done when she was 7 because of a pyuria of four months. The right kidney urine contained clumped pus. The left kidney urine was normal. The right kidney pelvis was lavaged with mercurochrome. Her health improved and she was well until Nov. 11, 1939, when she complained of a dull ache in her left loin. On November 13 she complained of severe occipital headache. Within the next twenty-four hours she was seized with several short convulsions, became unconscious and was admitted to the Woman's General Hospital in Montreal. There were no urinary symptoms. Cystoscopic and pyelographic studies were made showing an atrophic right kidney and a large left kidney. Her blood pressure varied between 180 and 140 systolic, and 135 and 105 diastolic. A right nephrectomy was done on December 27. The pathologic diagnosis was chronic pyelonephritis with secondary atrophy of the kidney, arteriosclerosis, hydronephrosis and chronic ureteritis. There was no appreciable change in the patient's blood pressure up to the time she left the operating table. One hour afterward it was 150; two hours after operation it was 115 systolic and 95 diastolic. During the next twenty-four hours the systolic pressure averaged 125. Following an intravenous infusion of dextrose-saline solution the blood pressure rose to 165 systolic and 130 diastolic and during the next twenty-four hours it gradually fell to 120 systolic and 90 diastolic. She was discharged from the hospital seventeen days after operation. Her blood pressure seemed to be stabilized at 90 systolic and 60 diastolic. She has remained well and without complaints. On the date of her last examination, June 4, she had gained 20½ pounds (9.3 Kg.) in weight. At this time the blood pressure was 96 systolic and 60 diastolic. The authors collected from literature 22 cases in which unilateral nephropathy was associated with hypertension and in which definite improvement followed nephrectomy. Numerous other cases have been mentioned, but with insufficient data to warrant inclusion. Of the 23 cases, 5 occurred in children of 12 or less years of age.

Gentian Violet for Pinworm Infection.—Miller and his collaborators used gentian violet tablets in the treatment of 29 school children, from 6 to 13 years of age, positive for pinworms by the National Institute of Health anal swab technic. The gentian violet was administered in ½ grain (0.03 Gm.) and 3/20 grain (0.01 Gm.) tablets. The disintegration of the tablets used was supposed to occur four hours after they were swallowed, thus providing the largest concentration of the drug at the site of the infection. Treatment was continued for ten consecutive days. Children from 6 to 9 years of age were given two 3/20 grain tablets three times a day before each meal and children from 10 to 13 years of age were given one ½ grain tablet three times a day before each meal. One week following the completion of the treatment an anal swab was made on each patient and two others at weekly intervals. Of the 29 children who took the prescribed dosage and had three post-treatment swabs, only 3 were found still positive following treatment. The effects of gentian violet could be studied on 31 patients taking the entire prescribed dosage. Of these, 23 reported no ill effects, 2 reported slight abdominal pain, 3 slight nausea lasting only one day, 1 anorexia lasting one day, 1 anorexia lasting for several days and 1 colicky pains with nausea. No child in the age group tested and taking the prescribed dosage vomited. However, 2 children (1 and 8 years old was inadvertently given the higher dosage and the other child's dosage was halved) vomited and had anorexia. Both of these children were underweight and had poor appetites, and the smaller child was extremely nervous. The symptoms were usually so mild that treatment was not interrupted with the exception of 4 patients whose symptoms disappeared and did not return with the resumption of treatment.

Fatal Serum Reaction.—Ferguson cites the case of a boy of 6 years who was given 3 minims (0.18 cc.) of tetanus antitoxin because of many deep abrasions covered with street dirt as a result of a car accident. The antitoxin was given at 3:05 p. m., at 3:07 sodium salt of *n*-methyl-cyclohexenylmethyl malonylurea was started intravenously, and in eight minutes 5.5 cc. had been given, which was thought to be enough. There had been no premedication and the patient went to sleep quite easily with some slight twitching. There was no appreciable change in the pulse and only slightly shallower respiration. The color remained good. At 3:20 the patient suddenly began to have trouble getting air into the lungs and would not breathe, although the passage was free. The chest was held in a tightly

contracted state of full inspiration. Artificial respiration was begun and 5 minims (0.3 cc.) of epinephrine was given subcutaneously. The pulse remained strong. At 3:30 a large wheal was noticed at the site of the intradermal injection of the tetanus antitoxin. The whole flexor surface of the forearm from the wrist to the elbow was reddened and edematous. The pulse was becoming irregular and 10 minims (0.6 cc.) of epinephrine was injected subcutaneously, followed by 1.7 cc. of a 25 per cent solution of pyridine betacarbonic acid diethylamine intravenously. The pulse improved appreciably following this. At 3:45 the pulse again became weaker and 5 per cent dextrose in saline solution intravenously was started. The patient began to take spontaneous breaths of a forced inspirational character and at 3:50 respirations were beginning to be of a more normal character. Large quantities of frothy, blood stained fluid began to pour from the lungs. The intravenous injection was stopped after 350 cc. had been given and the patient was placed in the Trendelenburg position to facilitate drainage. At 4:25 the patient's condition was much improved. Oxygen was being administered continuously through the endotracheal catheter. At 5:30 the patient suddenly stopped breathing and could not be revived. Death was considered to be due to anaphylaxis. The postmortem diagnosis after necropsy was serum reaction (accelerated) with pulmonary edema.

Journal of Immunology, Baltimore

39:265-368 (Oct.) 1940

Immunologic Reactions in Poliomyelitis. S. Raffel and E. W. Schultz, Stanford University, Calif.—p. 265.
Comparison of Various Physical Means of Liberation of Agglutinogen from Haemophilus Pertussis in Phase I. E. W. Flosdorf and Anne C. Kimball, Philadelphia.—p. 287.
Studies on Detectability of Pneumococcic Capsular Polysaccharide in Urine: Influence of Variations in PH. P. F. de Gara and S. C. Bukantz, New York.—p. 297.
Determination of Optimal Ratio of Cholesterol to Tissue Extract Antigen in Complement Fixation Test for Syphilis. J. F. Kent, Albany, N. Y.—p. 307.
Proteins and Antibodies of Serum After Prolonged Dialysis: I. Periodic Removal of Precipitates. S. Raffel, C. F. Pait and M. C. Terry, Stanford University, Calif.—p. 317.
Id.: II. Dialysis Without Periodic Removal of Precipitate. S. Raffel and M. C. Terry, Stanford University, Calif.—p. 337.
Id.: III. Serial Immunization with Quantitative Antibody Estimations. S. Raffel and M. C. Terry, Stanford University, Calif.—p. 349.
Hemolytic Effect of Typhoid Cultures in Combination with Pure Lines of Bacteriophage. F. Schiff and S. Bornstein, New York.—p. 361.

Journal of Investigative Dermatology, Baltimore

3:347-442 (Oct.) 1940

Hereditary Influences in Psoriasis. C. Lerner, New York.—p. 347.
Nails and Nail Changes: III. Brittleness of Nails (Fragilitas Unguium). H. Silver and B. Chiego, New York.—p. 357.
*Studies of Transmissibility of Syphilis: Infectiousness of Vaginal Secretions and Menstrual Blood of Syphilitic Women. H. Pariser, Philadelphia.—p. 375.
Studies with Antigens: VI. Significance of Scratch Test Reactions to Purified House Dust Extracts. B. G. Efron, C. H. Boatner and M. R. Pabst, New Orleans.—p. 401.
Value of Liver Extract in Cases Intolerant to Arsenicals, Heavy Metals and Radiation. G. M. MacKee and G. D. Astrachan, New York.—p. 409.

Transmissibility of Syphilis.—Pariser investigated the infectiousness for rabbits of the vaginal secretions and menstrual blood of 30 untreated syphilitic women. The biologic method of animal inoculation used is detailed. The author considered a result positive only when the injected material produced a syphiloma containing many spirochetes. The vaginal secretions of 7 women produced syphilis in animals. Five of these showed local cervical lesions. The clinical manifestations of the disease in these instances varied from about one week to six and one half years. The sixth positive result was obtained from the menstrual blood of a woman with secondaries who had no local cervicovaginal lesions, and the seventh from an early secondary syphilitic pregnant woman whose cervix was edematous, bluish and boggy but with no visible open lesions. How much of this cervical picture was due to the pregnancy is difficult to determine. It might have been the type of early lesion stressed by Stookey, Davies and MacDonald. Initial dark field examination revealed a few organisms which closely conformed to the universally accepted morphology of Spirochaeta pallida in 4 cases, slightly thicker organisms than average but which by subsequent animal inoculation were proved to be Spirochaeta pallida in 2 instances while the seventh case was negative. In the absence of lesions the dark field examination in 50 per cent of the cases revealed spirochetes easily distinguished from Spirochaeta pallida. The case material consisted of 76 per cent early syphilis and 24 per cent late syphilis. Serologic tests for syphilis in rabbits gave, with certain modifications, high sensitivity ratings but also produced a definite percentage of nonspecific positive serologic tests. These tests should be used only as collateral evidence and only the appearance of a syphiloma containing many spirochetes should be diagnostic. The author concludes that virulent spirochetes are discharged in the syphilitic woman into the vagina in the presence of early or chronologically late (more than four years) local lesions as a relapsing phenomenon. In the absence of such lesions in the early syphilitic woman they are discharged through the menstrual blood or from an abnormally appearing cervix in which it is probable that lesions are present within the cervical os or uterus. Infectiousness through the vagina is periodically recurrent rather than continuous and depends on the presence or absence of local lesions. The physiologic secretions are not infectious. The absolute end point or the frequency of cervical relapse cannot be given, but the author states that in his cases infectious cervical relapse occurred at least six and a half years after definite onset of the disease.

Journal-Lancet, Minneapolis

60:479-522 (Nov.) 1940

Subdural Hematoma. A. L. Sahs, Iowa City.—p. 479.
Surgery of Gallbladder Tract, Based on Understanding of Physiologic Functions and Pathologic Changes that Take Place in the Liver. W. A. Delaney, Mitchell, S. D.—p. 482.
Eye Health Among College Students. J. H. Kler, New Brunswick, N. J.—p. 487.
Blood Transfusions in Pediatrics. W. S. Sako and A. V. Stoesser, Minneapolis.—p. 491.
Summary of a Ten Year Tuberculosis Control Program. L. S. Jordan, Granite Falls, Minn.—p. 502.
Spontaneous and Surgical Covering of Raw Surfaces. J. B. Brown and L. T. Byars, St. Louis.—p. 503.

Journal of Urology, Baltimore

44:389-544 (Oct.) 1940

Primary Echinococcosis of Kidney. W. A. Barrett, Pittsburgh.—p. 389.
*Bilateral Renal and Ureteral Agenesis. K. B. Grim, Charlottesville, Va.—p. 397.
Renal Tuberculosis and Sanatorium Care. F. H. Colby, Boston.—p. 401.
Retro-Aortic Renal Vein. G. Yelin, Newark, N. J.—p. 406.
Renal Vascular Pedicle: Anatomic Study of 430 Body Halves. J. W. Pick and B. J. Anson, Chicago.—p. 411.
Relationship of Benign and Malignant Hypernephroid Tumors of Kidney: Clinical and Pathologic Study of 77 Cases in 12,885 Necropsies. D. D. Kozoll and J. D. Kirshbaum, Chicago.—p. 435.
Retrocaval Ureter: Report of Case with Operative Correction of Defect. H. C. Harrill, Greensboro, N. C.—p. 450.
Operative Technic in Treatment of Vesical Diverticula. H. H. Young, Baltimore.—p. 458.
Vesical Diverticulectomy. J. E. Dees, Durham, N. C.—p. 466.
Contracture of Bladder: II. Elastosis of Bladder. J. H. Winer, Cleveland.—p. 485.
Prostatic Obstruction as Presenting Symptom of Acute Monocytic Leukemia. S. A. Flaherty, Detroit; H. E. Cope, Lansing, Mich., and H. A. Shecket, Eloise, Mich.—p. 488.
Frequency of Tubercle Bacillus in Urine of Chronic Pulmonary Tuberculosis in Relation to Urogenital Complications. Esther Rosencrantz, San Francisco.—p. 498.
Clinical Study of 480 Cases of Urinary Lithiasis. H. L. Harrington, San Francisco.—p. 507.
Effect of Intraprostatic Injection of 1 and 1.5 per Cent Aqueous Mercurochrome into Prostates of Dogs. L. W. Riba, B. W. Milligan and F. B. Queen, Chicago.—p. 520.
Content of Male and Female Hormone in Urine of Patients with Prostatic Hypertrophy. Elisabeth Dingemanse and E. Laqueur, Amsterdam, Netherlands.—p. 530.
Use of Sulfathiazole and Sulfamethylthiazole in Treatment of Gonorrheal Urethritis. T. M. Burkholder and F. Bang, Baltimore.—p. 541.

Bilateral Renal and Ureteral Agenesis.—Grim cites a case of bilateral renal and ureteral agenesis in the presence of an otherwise normal urogenital system and with no demonstrable developmental defects elsewhere. The patient's mother, a 32 year old multipara, went through a normal gestation until two days before admission to the hospital, when she had abdominal cramps radiating anteriorly from both flanks. No fetal movements could be felt and no heart sounds heard. Several hours after admission she was delivered of an apparently normal

but slightly macerated stillborn fetus approximately 8 months old. Careful examination of the umbilical cord and placenta revealed no abnormalities. Necropsy of the infant revealed no abnormalities other than the absence of the kidneys and ureters. Embryologically this finding may be due to (1) failure of the ureteral bud to appear, (2) failure of the ureteral bud to develop or grow cephalad into the nephrogenic cap, (3) degeneration of the ureteral bud from any cause before it has contacted the nephrogenic cap, (4) failure of the nephrogenic cap to appear, (5) degeneration of the nephrogenic cap after its appearance and (6) defective germ plasm. The author points out that Ranier's contention that development of the metanephrogenic blastema depends on the stimulus evoked by cephalic progression of and contact with the ureteral bud seems to be borne out by the observations in his case. He believes the associated pathologic changes may be attributed to asphyxia in utero.

Medical Annals of District of Columbia, Washington

9:333-370 (Oct.) 1940

Inclusion Blennorrhea in Pediatric Practice. S. W. Giddens, Toronto, and W. A. Howard, Washington.—p. 333.
Prenatal Care. H. F. Kane, Washington.—p. 342.
Failures and Recurrences Following Estrogen Treatment of Gonorrheal Vulvovaginitis. B. Notes, Washington.—p. 346.
Value of Roentgenography in Diagnosis and Localization of Intestinal Obstruction. A. M. Cove, Brooklyn, and M. Silverman, Washington.—p. 348.

Military Surgeon, Washington, D. C.

87:289-400 (Oct.) 1940

Surgical Pathology of Acute Infections of Maxillofacial Area: Clinico-Anatomic Study. M. W. Carr.—p. 289.
Infantile (Acquired) Hernia at Umbilicus in Soldiers. H. H. Parsons.—p. 298.
Intravenous Anesthesia and How to Use It. R. B. Phillips.—p. 301.
Experimental Aircraft-Submarine Litter and Transportation Splints. W. L. Mann and R. Kaysen.—p. 305.
Mechanized Medical Units. C. M. Hendricks.—p. 311.
Thoraco-Abdominal Syndromes. M. B. Shimkin.—p. 316.
Acute Gangrenous Diverticulitis (Meckel's) with Perforation Due to Fish Bone: Case. J. M. Tamraz.—p. 328.
Short Wave Diathermy. L. De Forest.—p. 330.
Allergy in Military Medicine. F. G. Crandall Jr.—p. 337.
Early Panama Crossing. J. M. Phalen.—p. 352.

Nebraska State Medical Journal, Lincoln

25:393-428 (Nov.) 1940

Present Social Trends and Future of Medicine. E. J. McCormick, Toledo, Ohio.—p. 393.
*Intramuscular Administration of Sodium Sulfapyridine: Preliminary Report. L. T. Hall, C. E. Thompson and R. J. Wyrens, Omaha.—p. 398.
Impalement of Rectum with Intra-Abdominal Rupture: Report of Three Cases. M. C. James, Columbus.—p. 399.
Treatment Facilities in the State Mental Hospitals in Nebraska. J. C. Nielsen, Ingleside.—p. 403.
Traumatic Surgery as a Specialty. T. E. Riddell, Scottsbluff.—p. 409.
Practical Consideration of Antianemic Drug Therapy: Uses and Abuses. J. C. Sharpe, Omaha.—p. 413.
Simultaneous Rupture of Left Kidney and Spleen: Case Report. P. S. Adams and W. F. Bowers, Omaha.—p. 417.
Standards for Judging a Member of a Profession—The Physician. E. C. Sage, Omaha.—p. 419.

Sodium Sulfapyridine Intramuscularly.—Hall and his associates observed no local irritation or tumefaction after many deep intramuscular administrations of sulfapyridine. The clinical effects were equal to those obtained by other routes. Blood levels of from 3 to 10 mg. per hundred cubic centimeters were promptly obtained. Once the level is reached it can be maintained for longer periods than when given intravenously. Gastrointestinal reactions are almost entirely avoided, nausea does not occur and vomiting is seldom observed. This route may be found to be a safe alternative for intravenous injection in old persons with tortuous and sclerotic vessels, in infants, children and women with inconspicuous veins, or in persons with fat arms. The authors used a 33⅓ per cent solution of sulfapyridine in sterile water, injecting it deep into the gluteal or thigh muscles. No material must be deposited in the subcutaneous tissue through the needle tract either on injection or during withdrawal of the needle. Each cubic centimeter of the solution contains 0.33 Gm. of the drug. From 6 to 10 cc. was given as the first injection and was followed by 3 cc. every four hours until the temperature had been normal for twenty-four hours. Thereafter the dose was reduced by one half and continued for the next five or six days. This route has been used for pneumonia, undulant fever, appendicitis with peritonitis, abscesses, pyelitis, typhoid, gonorrhea, sinusitis and many other diseases. The authors state that the clinical results parallel those obtained by orally administered sulfapyridine.

New York State Journal of Medicine, New York

40:1419-1486 (Oct. 1) 1940

Diagnosis of Serious Urologic Conditions. H. H. Young, Baltimore.—p. 1425.
Treatment of Epithelial Tumors of Bladder with Radiation. A. L. Dean and J. Balfour, New York.—p. 1431.
Treatment of Tumors of Bladder by Refrigeration. A. McCravey, Philadelphia.—p. 1435.
General Considerations in Surgical Treatment of Carcinoma of Bladder, with Particular Reference to Total Cystectomy. J. T. Priestley, Rochester, Minn.—p. 1441.
Administration of Sulfapyridine and Its Congeners in Pneumonias. J. G. M. Bullowa, H. D. Ratish, A. Davidson and Constance Lebair, New York.—p. 1450.
Influence of Sulfapyridine on Pneumonias of Childhood: Clinical Study of Eighty-Five Cases at a Municipal Hospital. S. L. Ellenberg and H. S. Altman, New York.—p. 1457.
Survey of Eighteen Years of Pneumonia at the Nassau Hospital. B. R. Allison, Hewlett.—p. 1464.

40:1487-1556 (Oct. 15) 1940

Participation in Public Health Program: Public Health Personnel. V. A. Van Volkenburgh, Albany.—p. 1493.
The Place of the Medical Profession in the Public Health Program. A. N. Thomson, Brooklyn.—p. 1498.
The Citizen. K. D. Widdemer, New York.—p. 1501.
The School Physician in the Public Health Program. G. M. Wheatley, New York.—p. 1506.
Aseptic Total Colectomy. D. P. MacGuire, New York.—p. 1515.
Hyperactive Carotid Sinus Reflex Syndrome. A. Koffler and S. F. Alexander, New York.—p. 1519.
Sulfapyridine in Meningococcic Meningitis: Review of Literature and Report of Case. H. I. Kantor, New York.—p. 1526.
Obstetric Prognosis and Treatment on Basis of Pelvic Architecture. A. Weinberg, Far Rockaway.—p. 1530.

South Carolina Medical Assn. Journal, Greenville

36:301-330 (Nov.) 1940

Chronic Conditions of Gallbladder. Gertrude Holmes and H. Smith, Greenville.—p. 301.
Surgical Management of Varicose Veins and Ulcers. H. G. Smithy, Charleston.—p. 307.

Southern Medical Journal, Birmingham, Ala.

33:1117-1240 (Nov.) 1940

Reticulo-Endotheliosis. J. H. Lamb and H. A. Stout, Oklahoma City.—p. 1117.
Use and Abuse of Theophylline and Its Derivatives. A. McMahon and R. A. Nussbaum, St. Louis.—p. 1127.
Role of Streptococcus in Some Dental Infections: Study of Residual Areas. Iva C. Youmans and Laura M. Hobbs, Miami, Fla.—p. 1140.
Controlled Rotation Osteotomy of Tibia. D. H. O'Donoghue, Oklahoma City.—p. 1145.
Isolated Bilateral Fracture of First Rib: Case with Unilateral Horner's Syndrome. J. Kulowski and J. H. Ryan, St. Joseph, Mo.—p. 1149.
*Placenta Accreta: Case Report. C. E. Bosshardt, San Antonio, Texas.—p. 1152.
Pyuria: Its Significance in Upper Urinary Tract Disease. H. J. Lindner, New Orleans.—p. 1155.
Treatment and Prevention of Deafness in Children. J. E. Bordley, Baltimore.—p. 1159.
Cataract Attributable to Use of Dinitrophenol. A. O. Pfingst, Louisville, Ky.—p. 1164.
Epidemic Diarrhea of Newborn. T. G. Folsom and G. M. Lyon, Huntington, W. Va.—p. 1167.
*Report of Two Ruptured Gastric Ulcers and One Ruptured Duodenal Ulcer in Three Newborn Infants. A. G. Quinn, Memphis, Tenn.—p. 1171.
Dihydrotachysterol, Parathormone and Vitamin D_2: Comparison of Their Values; Treatment of Post-Thyroidectomy Hypocalcemic Tetany. D. H. Poer, Atlanta, Ga.—p. 1174.
Comparison of Skin Reactions Obtained by Use of Brucella Nucleoprotein (Brucellergen) and Heated Brucella Organisms in Sensitized Individuals. A. E. Keller, Nashville, Tenn.—p. 1180.
Therapeutic Effects of Aminophyllin in Asthma. A. G. Brown 3d and W. B. Blanton, Richmond, Va.—p. 1184.
Relationship of Personality Changes to Facial Neuralgia. M. S. Love and D. C. Wilson, University, Va.—p. 1186.
Cause and Prevention of Loss of Teeth. C. C. Bass, New Orleans.—p. 1193.
Birth and Early History of the Southern Medical Association. J. L. Crook, Jackson, Tenn., and W. W. Crawford, Hattiesburg, Miss.—p. 1195.

Placenta Accreta.—Bosshardt states that placenta accreta is being seen and recognized more frequently as the most serious complication of the third stage of labor. The condition results from a partial or complete absence of decidua basalis. Placenta

accreta must never be confused with the rather common simple placental retention seen in hour-glass constriction or from some failure of the normal separating mechanism of a healthy placenta in a normal uterus. Since this condition can never be detected before delivery, it should be constantly kept in mind after the second stage of labor. Treatment depends on prompt recognition. Early hysterectomy is the accepted treatment, preceded and followed by blood transfusion, if indicated, and the usual supportive agents for shock. Manual extraction of densely adherent placentas by hand, with placental forceps or by curet is extremely dangerous and predisposes to fatal hemorrhage or puncture of the uterus. In 11 cases treated by supravaginal hysterectomy with no attempts at extraction of the placenta there were no deaths. There were 6 deaths among 30 cases in which abdominal hysterectomy after partial manual extraction was employed. Manual extraction or curettage without hysterectomy for 31 cases resulted in 20 deaths. The combined mortality of the treated series reported in 1931 showing 86 cases with 32 deaths was 37.2 per cent. The author's cases bring the total to 101. His patient, even after procrastination for nine days and adopting the hazardous method, unknowingly, of partial manual extraction, recovered after a subtotal hysterectomy.

Ruptured Ulcers in Infants.—Quinn reports 3 fatal cases of ruptured gastrointestinal ulcers in infants. Two of them occurred during a year when there was an epidemic of infectious diarrhea. One of these, the author believes, can be said to have occurred from this cause. The following diagnostic criteria stand out: First, pneumoperitoneum was determined by roentgen study, yet this failed in the first case so examined. The other diagnostic point was that abdominal distention occurred suddenly in an otherwise healthy infant. The distention was symmetrical and had the feel and appearance of an inflated round bag. The principal features of the first case were an infant doing well who vomited following a feeding and four hours later vomited again. The abdomen was markedly distended, giving the appearance of an inflated ball. Attempts to relieve distention were unsuccessful. Respiratory distress, cyanosis and shock were present. In the second case, because of sudden vomiting, abdominal distention and shock, the presumed diagnosis was ruptured gastrointestinal ulcer, but because pneumoperitoneum was absent on roentgen study the preoperative diagnosis was intestinal obstruction. The operative observations proved the first premise correct, yet no pneumoperitoneum was present. The third infant died five days after operation. The anatomic diagnosis was primary, perforated acute peptic ulcer (clinical), generalized fibrinous purulent peritonitis and bilateral bronchopneumonia. The cause of death was bronchopneumonia.

Tennessee State Medical Assn. Journal, Nashville

33:419-458 (Nov.) 1940

Treatment of Wounds of Face. R. A. Daniel Jr., Nashville.—p. 419.
Treatment of Fractures of Neck of Femur. E. D. Newell, J. M. Frere and J. M. Higginbotham, Chattanooga.—p. 427.
Head Injuries. R. G. Waterhouse, Knoxville.—p. 432.
Treatment of Injuries of Chest. D. Carr, Memphis.—p. 438.

Virginia Medical Monthly, Richmond

67:655-716 (Nov.) 1940

Management of Acute Appendicitis: Arguments and Controversies. H. B. Stone, Baltimore.—p. 655.
Treatment of Sinusitis. W. C. Bowers, New York.—p. 660.
Degenerative Neuropsychiatric Conditions Due to Aging Process. R. S. Crispell, Durham, N. C.—p. 668.
Unusual Tumors and Tumor-like Lesions of Spinal Canal and Its Contents, with Special Reference to Pitfalls in Diagnosis. J. M. Meredith, Charlottesville.—p. 675.
Cysts of Maxillary Sinus. T. E. Hughes and J. S. Dryden, Richmond.—p. 687.
Treatment of Ulceration of Foot in Advanced Arteriosclerosis. B. L. Boynton, Norfolk.—p. 689.
Chronic Atonic Dilatation and Hypersecretion of Stomach Successfully Treated with Insulin. W. J. Mallory, Washington, D. C.—p. 691.
Foreign Body Simulating Gastric Carcinoma. B. Lidman, Norfolk.—p. 693.
Venesection in Pulmonary Edema: Case Report with Discussion of Diagnosis, Etiology and Treatment. G. Geyerhahn, Wilmington, N. C.—p. 696.
Perforated Peptic Ulcer and Recovery Without Operation. H. G. Hadley, Washington, D. C.—p. 697.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

48:591-644 (Oct.) 1940

*Pyelitis of Pregnancy and Its Management in 121 Cases. R. D. Mussey and S. B. Lovelady, Rochester, Minn.—p. 591.
Simple Method of Therapeutic Abortion Combined with Sterilization. H. C. Falk and A. Shukuris, New York.—p. 597.
Obstetric Forceps. C. H. Davis, Wilmington, Del.—p. 601.
Use of Testosterone Propionate in Gynecologic and Obstetric Disorders. T. E. Mandy and A. J. Mandy, Baltimore.—p. 604.
Dangers and Uses of Radium in Treatment of Carcinoma of Uterus. M. D. Sachs, Portland, Ore.—p. 609.
Kahr Operation for Senile Prolapse. J. H. Clark, Los Angeles.—p. 616.
Surgical Pathology of Thyroid Gland. A. C. Broders, Rochester, Minn.—p. 620.
Further Observations on Thyrotropic Activity of Anterior Pituitary. W. O. Thompson, Phebe K. Thompson and S. G. Taylor 3d, Chicago.—p. 633.
The Heart in Hyperthyroidism. E. J. Kepler, Rochester, Minn.—p. 636.

Pyelitis of Pregnancy and Its Management.—According to Mussey and Lovelady, among 5,960 deliveries at the Mayo Clinic 117 were complicated by pyelitis. Four others have been encountered since the introduction of sulfanilamide. Seventy-two of the patients were primigravidas and forty-five multigravidas, bearing out some previous reports that pyelitis occurs more frequently among the former. There were ninety-two instances of antepartum and twenty-five of postpartum pyelitis. Postpartum pyelitis was usually of mild degree and did not exhibit the usual symptoms of pyelitis of pregnancy. Previous infection of the upper part of the urinary tract plays a part in the recurrence of pyelitis in subsequent pregnancies; however, only twelve of the present patients gave a history of pyelitis prior to the first pregnancy and none gave a history of urinary infection in childhood. The data of the 117 cases do not confirm the assertion that pyelitis increases the hazard of pregnancy. There were four spontaneous abortions and two premature labors. Labor was induced because of pyelitis in seven cases, but not before viability. One of 117 patients died. Acute pyelitis was rarely the cause of preeclamptic toxemia or eclampsia among the series discussed. Although pyelitis is not a common complication of pregnancy it occurs with sufficient frequency to necessitate alert diagnosis and treatment before permanent renal damage occurs. Whenever pus is found in a specimen of urine during periodic prepartum examination a specimen of urine obtained by catheterization should be examined for pus, for pyelitis without subjective symptoms may be present. The 121 patients have been divided into four groups. Group 1 received large quantities of fluids and usually one of the urinary antiseptics, group 2 was treated by ureteral catheter drainage, group 3 was given one of the various mandelic acid preparations and group 4 includes the four patients given sulfanilamide. The results of administrating large quantities of fluid to sixty-four patients were uniformly good and indicate that in more than one half of the cases pyelitis of pregnancy will respond favorably to forced fluids and rest in bed. These measures were most effective when applied early in the course of the disease. In group 2, forty-eight patients, there were acutely ill patients who failed to respond to the treatment outlined in group 1, and indwelling catheters were inserted for adequate drainage of the renal pelvis. From 1924 to 1933 ureteral drainage was used in approximately 57 per cent of patients with proved pyelitis of pregnancy. Since 1933 this treatment has been employed in approximately 19 per cent of the cases. When pyelitis of pregnancy is recognized and treated in its early stages, a majority of patients will recover following a regimen of rest in bed, sedatives and forced fluids. The effect of this management has been a continuing decrease in the number of patients requiring ureteral catheterization. Since the advent of chemotherapy, this will no doubt become still less. The only death of the entire series occurred in this group. Mandelic acid was used for the five cases of group 3, and the response to treatment was uniformly good. The response of the four patients of group 4 to sulfanilamide was good. Further observation may indicate the advisability of employing azosulfamide or other allied products. The average duration of fever and hospitalization of the groups of patients was, respectively, fever 3.6, 6.8, 3.0 and 5.0 days, and hospitalization 10.7, 10.8, 14.0 and 13.0 days.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Journal of Mental Science, London

86:751-1064 (Sept.) 1940

Diphasic Vascular Variation in Treatment of Mental Inefficiency Arising from a Common Somatic Cause. T. C. Graves.—p. 751.
Role of Sex Hormones in Psychiatry. M. Reiss.—p. 767.
Specific Psychotic Reaction of Schizophrenics to Physical Illness. R. E. Hemphill and E. Stengel.—p. 790.
Studies in Certain Pathophysiologic and Psychologic Phenomena in Convulsion Therapy. R. E. Hemphill.—p. 799.
Cerebral Fat Embolism as Cause of Death in Case of Schizophrenia Treated with Triazol (Azoman). G. S. Nightingale and A. Meyer.—p. 819.
Forced Grasping and Disturbances of Attention. B. Schlesinger.—p. 827.
Morbid Attention: Factor in Nervous Disorder. I. C. K. Mackenzie and Ivy Mackenzie.—p. 839.
Modern Treatment of Epilepsy: Critical Survey, with Special Reference to Sodium Diphenyl Hydantoinate and Comparison of Its Effects with Those of Other Anticonvulsants. D. Blair.—p. 888.
Psychotherapy in Mental Hospital Practice: Being the Preliminary Report of a Full Time Psychotherapist in a Public Mental Hospital. J. Bierer.—p. 928.
Commentary on Case of Acute Systematized Hallucinosis: Recorded by the Patient as "The Report of a Nightmare." M. J. Nolan.—p. 953.
Some Points in Technic of Insulin Therapy of the Psychoses. R. Fraser and W. Sargant.—p. 969.
Severe Toxic Effects of Sodium Diphenyl Hydantoinate in Mentally Defective Epileptics. B. A. M. Williamson.—p. 981.
Recent Hysterical States and Their Treatment. A. Kennedy.—p. 988.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

47:365-492 (Aug.) 1940

Cold Pressor Test in Pregnancy. F. J. Browne.—p. 365.
External Hysterography: Graphic Study of Human Parturient Uterus and Effect of Various Therapeutic Agents on It. M. P. Embrey.—p. 371.
Investigation into Result of Operation in Genital Prolapse. J. Stallworthy.—p. 391.
Eclampsia: Clinical and Biochemical Study: Part II. Biochemical Investigation of Eclampsia. A. S. M. Nayar.—p. 404.
Calcification of Human Placenta. M. Masters and S. G. Clayton.—p. 437.
Treatment of Retroversion of Uterus: Impression of Present Position from Analysis of Cases Undergoing Operation at Samaritan Hospital, London. A. H. Charles.—p. 444.
Desmoblastoma Ovarii Malignum. B. Solomons and G. C. Dockeray.—p. 451.
Unusual Case of Breech Presentation of Eight Months' Pregnancy Complicated by Tubo-Ovarian Abscess. V. R. Merajkar and B. L. Kapur.—p. 455.

47:493-596 (Oct.) 1940

Relaxation of Pelvic Joints in Pregnancy: Pelvic Arthropathy of Pregnancy. J. Young.—p. 493.
Inversion of Uterus. P. Das.—p. 525.
Prognosis for Fetus in Toxemias of Late Pregnancy. F. J. Browne and Gladys H. Dodds.—p. 549.
Retroperitoneal Cyst Containing Ovarian Remnants: Case. S. Way.—p. 553.
*Cyclic Ulcerative Vulvitis and Stomatitis. O. V. Jones.—p. 557.
Tubo-Uterine Implantation Followed by Successful Pregnancy. S. Hayes.—p. 563.

Cyclic Ulcerative Vulvitis and Stomatitis.—Jones points out that numerous cases of coexisting oral and genital ulceration have been reported but that only 3 of these seemed to have any relation to menstruation. He reports the fourth case of such an association. The clinical similarity between the genital and oral ulcers is striking, and so it is probable that the ulceration of the two areas has the same pathology. Since the original observation by Neumann in 1895 the etiology of their association has excited much discussion and at present there are three main theories: that of an acute infectious disease of bacterial origin, a condition analogous to the tuberculoids, and that of angioneurotic gangrene due to ovarian dysfunction. The first two theories fail to become established. The ovarian dysfunction theory becomes feasible as in the cases reported and in the author's case the lesions were dependent on the menstrual cycle. The condition was associated in some way with the endocrine changes of menstruation. In the author's case the vulvar lesion commenced from one to two weeks before menstruation, lasting over the period but ceasing after menstruation, while the oral lesion occurred from one to two days before, during or after menstruation. The striking appearance and disappearance of the lesions with a regular relation to menstruation is highly suggestive of an endocrine dysfunction as an etiologic factor. There are microscopic changes (proliferation of the stratum germinativum, with increase in the number of young epithelial cells in the basophilic zone of the epithelium, and this is associated with occasional mitosis and a definite leukocytosis and hyperemia) in the vagina related to the hormone changes of menstruation. The fact that the time of these changes coincides with the ulcerative phase in the condition under discussion further enhances the endocrine basis. Since these ulcers appear at the premenstrual period when the secretion of estrogen is highest and disappear at the postmenstrual phase when it is lowest, a deficiency of estrogen is probably not the etiologic factor, and it is unlikely to be due to an excess of estrogen as the phenomena disappear during pregnancy. On the other hand, the lesions are present during the stage when the pituitary normally lessens its production of gonadotropic substance and its absence is coincident with the interval when anterior pituitary reaches its maximal concentration. Likewise during pregnancy (as in 1 case) when the anterior pituitary hormone attains its highest degree of activity there was a spontaneous disappearance of the ulceration. Therefore it seems reasonable that a lowered pituitary activity may cause the condition. Ziserman reported great improvement in his case after administration of an anterior pituitary preparation. In the author's case complete relief was obtained with gonadotropic substance, while after treatment was discontinued the symptoms returned. The patient did improve slightly on estrogen alone, but not until the anterior pituitary preparation was given was she completely free from both ulcerative lesions. Though the therapeutic trials suggest that deficiency of gonadotropic substance is the basic cause, the true underlying factors must still remain obscure. It is probably due to some systemic condition associated with an imbalance between various hormones. This is plausible, as the ulceration occurs at a time when there is a change in the cycle and when a harmonious cooperation between the hormones is necessary. Therefore any endocrine imbalance that occurs will reflect itself on the changes in the genitalia and general systemic system, and this will be more likely to occur in individuals whose vasodilatory system is easily affected, resulting in ulceration of the mucous membrane. The condition described is a definite syndrome and can be recognized as such when other factors (infection and anemia) have been eliminated. The disease differs from ulcus vulvae in that it is recurrent and rebellious to treatment and appears to be a systemic condition dependent on some dysendocrinism.

Journal of Pathology and Bacteriology, Edinburgh

51:169-316 (Sept.) 1940

Fundamental Lesion in Acute Diffuse Intracapillary Glomerulonephritis. J. S. Dunn.—p. 169.
Physiologic and Serologic Characteristics of Staphylococci of Human Origin. R. Christie and E. V. Keogh.—p. 189.
Toxin of Corynebacterium Ovis. H. R. Carne.—p. 199.
Medial Defects in Circle of Willis and Their Relation to Aneurysm Formation. L. E. Glynn.—p. 213.
Pathologic Changes Produced in Rats and Mice by a Toxic Fraction Derived from Bacterium Typhi Murium. G. R. Cameron, M. E. Delafield and Joyce Wilson.—p. 223.
Nature of Human Leukemia: Evidence from Culture of Bone Marrow Cells in Vitro. M. C. G. Israëls.—p. 235.
Pathogenicity and Toxicity of Bacterium Alkalescens for Laboratory Animals. D. G. f. Edward.—p. 245.
*Comparative Study of Anaerobic Strains of Actinomyces from Clinically Normal Mouths and from Actinomycotic Lesions. H. R. Sullivan and N. E. Goldsworthy.—p. 253.
Silicotic Nodule in Human and Experimental Silicosis: Comparative Study. T. H. Belt, A. A. Ferris and E. J. King.—p. 263.
Silica Content of Tissues, With and Without Silicotic Lesions. E. J. King and T. H. Belt.—p. 269.
*Pneumoconiosis in Coal Trimmers. J. Gough.—p. 277.
Importance of Suspending Fluid Used in Virulence Tests on Corynebacterium Diphtheriae. H. D. Holt and H. D. Wright.—p. 287.

Strains of Actinomyces from Normal and Actinomycotic Mouths.—In an investigation of patients with actinomycotic lesions in the cervicofacial region, Sullivan and Goldsworthy were impressed by the frequency with which actinomycosis appeared to be related to oral trauma, supporting the theory of endogenous infection. They have since examined material from the mouths of subjects with no history or clinical signs of actinomycosis and pus from cervicofacial lesions. From these they isolated anaerobic strains similar to Actinomyces bovis (Wolff and Israël) and compared these apparently nonpathogenic strains with those obtained from the lesions and with a strain from a subcutaneous abscess secondary to pulmonary actinomycosis. Five strains were isolated from periodontal

pockets (more than 100 were examined) and one from a carious tooth (twenty-four specimens were examined). Five other strains were isolated from lesions situated near the angle of the mandible, and one relatively old strain was obtained from the lesion secondary to pulmonary actinomycosis. In a comparative study which included fermentation reactions, these two groups of strains were identical. The results support the conclusions of other workers that the micro-aerophilic Actinomyces of Wolff-Israël is to be regarded as part of the normal flora of the oral cavity, at least if local dental conditions (caries and periodontitis) are accepted as practically universal. The authors' observations at dental clinics suggest that the acute form of actinomycosis is a not infrequent sequela to surgical manipulation of the mouth parts, especially the teeth. Therefore they believe that the organism leads a saprophytic existence in the mouth and invades the tissues only when conditions are rendered favorable, as by injury.

Pneumoconiosis in Coal Trimmers.—Gough states that in the last ten years fifteen coal trimmers have been encountered in routine postmortem work at the Cardiff Royal Infirmary. Three of these had previously been coal miners, but of at least five pneumoconiosis was the main cause of death. Coal trimming is the shifting and storing of coal on board ship in such a way as to make the vessel seaworthy. Most of the work is done in the ship's hold in an atmosphere thick with coal dust. The author's experience in Cardiff with steam coal leads him to conclude that exposure to these high concentrations for many years may lead to serious and sometimes fatal pulmonary fibrosis. One of the five men whose death was attributable to pneumoconiosis had a superadded pulmonary tuberculosis, and another had a limited carcinoma of the lung but the fibrosis and not the tumor was the cause of death. All in this group had been trimmers for more than twenty-five years. Three of the other men had severe pulmonary fibrosis but it was not the direct cause of their deaths. All had been trimmers for more than thirty years. The pulmonary fibrosis was slight in the other four men. They had been employed as trimmers for forty, thirty, seventeen and nine years, respectively. Like the pneumoconiosis of other industries, that of the coal trimmer shows fibrosis of two types—the discrete nodular and the massive or conglomerate. The massive type was present in the seven most severe cases. Microscopically the most prominent feature in the smallest nodule was the presence of abundant carbon. In the areas of massive fibrosis the parenchyma of the lung was completely replaced by dense fibrous tissue. The authors state that some clinical support to their observations has been furnished by Bathgate, who in his panel practice found clinical and x-ray evidence of pneumoconiosis in forty-four trimmers, eleven of whom were regarded as unfit for work owing to their pulmonary condition, and by Collis and Gilchrist, who reported in 1928 that coal trimmers in Cardiff often showed clinical and x-ray evidence of silicosis.

Medical Journal of Australia, Sydney

2:253-274 (Sept. 21) 1940

Interaction of Mind and Body. H. Ritchie.—p. 253.
Gonorrhea in the Male: Its Treatment and General Handling in the Community. W. F. Stephens.—p. 255.
Syphilis. K. McLean.—p. 258.

2:275-300 (Sept. 28) 1940

*Experimental Studies on Combined Sulfanilamide and Serum Treatment of Gas Gangrene Infections. E. Singer.—p. 275.
Anesthesia and Shock. S. V. Marshall.—p. 279.
Optical Convergence and Stereopsis in Relation to Perspective. J. Maude.—p. 281.
Artificial Hearing Aids. A. Bryant.—p. 283.
Statistical Study of Onset of Primary Dementia. J. F. Cade.—p. 285.

Sulfanilamide and Serum for Gas Gangrene Infections.—Singer investigated the protective power of sulfanilamides combined with antitoxic serum against experimental Clostridium welchii and Clostridium septicum infections. He also tried to increase the resistance of animals (mice) against the effects of the toxin with desoxycorticosterone. In a number of mice infected with soil suspensions and given a sufficient amount of the drug to cure an infection produced with pure culture of Clostridium welchii, postmortem studies revealed Clostridium welchii. This may mean that strains of Clostridium welchii differ in their susceptibility to the drugs or that mixed infection reduces their efficacy. Four strains of Clostridium welchii were used. Infection was produced by injecting subcutaneously into the tissues of the back twenty-four hour cultures of the particular anaerobe. Five equal doses of the drug were administered by stomach tube, two, four, seven, twenty-four and thirty-one hours after infection. The antitoxic serum was injected two hours after infection and immediately after the first dose of the drug. Considerable variation was encountered with different batches of mediums and different strains of organisms. Parallel experiments with groups of 4 mice show that more recently isolated strains seem to be more resistant to the drugs than the old laboratory strain S 107 used. The views of Stephenson and Ross that infections with strongly toxigenic strains were less responsive to chemotherapy were not substantiated as strain S 107, the most toxic strain, was the most susceptible to treatment. Tests with Clostridium histolyticum showed that sulfanilamides were completely inactive against it. The different sulfanilamides were about equally effective against infections with Clostridium welchii S 107 and with Clostridium septicum. Accordingly, only sulfanilamide and sulfapyridine were tested in conjunction with serum therapy. The amount of antitoxic serum administered was by itself inadequate to inhibit the course of the infection. Infections with multiples of one fatal dose were cured with relatively small quantities of drug combined with an amount of serum that by itself would be quite ineffective. This suggests that a similar form of therapy might be of considerable value in treating gas gangrene infections in the human being. The action of sulfanilamide drugs on Clostridium septicum infections was much weaker than on those of Clostridium welchii. However, much better results were obtained with the combined treatment. It seems that the better results with sulfanilamides plus serum treatment of Clostridium septicum infections are due, at least partly, to a kind of double action of the sulfanilamides on Clostridium septicum, while in Clostridium welchii infections the action of the drug limits itself to bacteriostatic and growth inhibiting effects. Some other mechanism not investigated in these experiments may be concerned. An attempt to treat fatal Clostridium oedematiens infections with a combination of drug and serum failed, as did treatment with drugs alone. Experiments with garden soil suspension infection and then treatment with the sulfanilamides and serum showed that all the deaths (11 of 20 mice used) were due to some cause other than the infection. A few experiments on mice showed that if treatment was delayed for from four to five hours after infection the possibility of cure was greatly lessened. In determining the effect of desoxycorticosterone against the toxin of Clostridium welchii, experiments were performed to show the action of the hormone against an immediately fatal dose of toxin and its influence on a chronic intoxication. Eight mice were given two daily subcutaneous injections of desoxycorticosterone (0.1 mg. in 0.1 cc. of sesame oil). On the second day 0.05 cc. of crude Clostridium welchii toxin (one fatal dose) was injected intraperitoneally. Eight mice, injected with toxin and pure sesame oil, served as controls. Of the mice treated with the extract 6 survived and only 1 of the controls survived. In another experiment 6 mice were given two daily injections of desoxycorticosterone before the Clostridium welchii toxin was administered. One third of a fatal dose of the latter was then given on five successive days and the administration of desoxycorticosterone was continued during this period. All the mice so treated survived, while only 2 of the control mice, injected with toxin and sesame oil, survived. Further research on the increase in resistance from desoxycorticosterone is indicated.

Practitioner, London

145:149-212 (Sept.) 1940

Menorrhagia. B. Whitehouse.—p. 149.
Diagnosis and Treatment of Salpingitis. H. J. D. Smythe.—p. 156.
Gynecologic Disorders of Puberty and Adolescence. Gertrude Dearnley.—p. 163.
Management of a Case of Prolapse. C. D. Read.—p. 169.
Some Common Ovarian Disorders. J. B. Blaikley.—p. 175.
Treatment of Burns. A. B. Wallace.—p. 180.
Plea for Modern Routine Anesthesia. E. V. Slaughter.—p. 188.
The Recruit's Heart: Preliminary Report. J. S. Lewis.—p. 192.
Injuries to Ear. S. Scott.—p. 197.
Modern Therapeutics: XV. Astringents. R. J. Rowlette.—p. 200.

Wiener klinische Wochenschrift, Vienna

53:597-616 (July 26) 1940

Newly Appearing Infectious Diseases and Methods of Combating Them. M. Gundel.—p. 597.
Lethal Factors. K. Keller.—p. 599.
*Question of Infectiousness of Icterus. F. Lainer.—p. 601.
Therapeutic Results and Prospects in Poisonings with Suicidal Intention. H. Seyfried.—p. 604.
Case of Rickets Between 1910 and 1920. H. Hücke! and R. Rheindt.—p. 606.
*Tuberculosis in Young Persons. O. Chiari.—p. 608.

Infectiousness of Icterus.—According to Lainer the only one form of jaundice in which the etiology is clearly established is Weil's disease caused by Spirochaeta icterogenes. The literature contains numerous reports of epidemics of jaundice in which the epidemic character was construed as evidence of its infectious nature. In other epidemics alimentary intoxication was cited as chief etiologic factor. Brugsch studied an epidemic of this type but was unable to detect a pathogenic organism. He suggested that these alimentary intoxications develop as the result of fermentative processes in the food, the fermentation producing dyspepsogenic and icterogenic substances which impair the liver. Other investigators raise the objection that the failure to detect a pathogenic organism does not exclude an invisible virus as possible cause. The large group of organisms belonging to the Bacterium typhi type have been connected with epidemics of jaundice, because of parallel appearance of the two, but investigations along this line have remained negative. As to sporadic or catarrhal icterus, although history here often reveals disorders of a toxic origin, many attempts have been made to ascribe to it an infectious cause. Icterus catarrhalis has been classified into three etiologic groups: (1) icterus simplex levis resulting from duodenitis with swelling of the papilla vateri, (2) icterus simplex duodenalis resulting from specific cholangitis and (3) icterus simplex hepatis resulting from diffuse parenchymatous impairment of liver by an infectious agent. Certain infectious diseases may play an icterogenic role. Attempts have been made, particularly by Andersen, to transmit catarrhal icterus to experimental animals. He obtained positive results in animal to animal and in man to animal experiments with the transmission of blood and of duodenal juice. Andersen's results induced the author to attempt transmission of catarrhal icterus from patients to animals by the feeding of duodenal juice and by blood transfusion, but extensive animal experiments failed to produce positive results. After several self experiments had remained negative the author made blood transfusions (300 cc. each) from fifteen patients with typical catarrhal icterus to persons without icterus. The duodenal juice was removed from these patients and introduced into healthy subjects. The serum bilirubin, the galactose elimination, the urobilinuria, the azorubin elimination in the duodenal juice were carefully examined in all the recipients of blood and duodenal juice, but none of them showed signs of hepatic impairment or of icterus. On the basis of these investigations the author concludes that the so-called icterus catarrhalis, whether sporadic or endemic, is the manifestation of a serous hepatitis produced by endogenic or exogenic toxins, but not by a specific icterogenic organism.

Tuberculosis in Young Persons.—Chiari stresses the susceptibility to tuberculosis during the puberal age and the importance of early diagnosis. The early recognition is difficult because the onset is often insidious. The general condition may be only slightly impaired and emaciation be entirely absent. Tuberculosis may simulate other disorders, for its manifestations are extremely varied. Every prolonged disorder in young persons should make the examiner think of tuberculosis. The family history is the first factor to be investigated. A case of open tuberculosis in the environment necessitates a careful search for tuberculosis. For this purpose three methods are of especial importance: the tuberculin reaction, x-ray examination and the demonstration of tubercle bacilli. If these methods are correctly utilized, it generally will be possible to detect a tuberculosis which requires treatment. The first aim of the treatment is the improvement of the patient's general condition, so as to strengthen the defense powers of the organism. Rest, fresh air and good food are of primary importance, while collapse therapy may be necessary in pulmonary tuberculosis and orthopedic measures in case of skeletal tuberculosis.

Acta Chirurgica Scandinavica, Stockholm

84:1-95 (June 29) 1940. **Partial Index**

Detritus Products in Joints and Their Reabsorption (Synovitis Detritica). O. Hultén and N. Gellerstedt.—p. 1.
*Differential Diagnosis in Gastric Hemorrhage. E. Ask-Upmark.—p. 30.
Intestinal Calculi in Meckel's Diverticulum. Å. Grevillius.—p. 37.
*Endometrial Implants in Small Intestine and in Navel: Case. A. Aronsson.—p. 43.

Differential Diagnosis in Gastric Hemorrhage.—Ask-Upmark discusses the diagnostic difficulties involved in determining the true cause of massive hematemesis. The clinical picture may be due (1) to a local process in the upper digestive tract, such as ulcer and carcinoma, (2) to stasis in the region of the portal vein, such as biliary cirrhosis, in which the esophageal varices constitute the hemorrhagic outlets, or thrombosis in the portal or splenic veins and (3) to a systemic disease with tendency to bleeding, such as malignant nephrosclerosis. Carcinoma rarely leads to excessive bleeding, yet, if accompanied by dyspepsia of recent date at the cancer age level, needs to be promptly examined roentgenologically despite the bleeding. Splenic thrombosis favors male subjects averaging between 20 and 24 years but is relatively rare, yet the spleen needs to be kept under constant observation during the course of the disease, as splenic enlargement may temporarily be abated, the blood finding an outlet through the ruptured ventricular branches of the splenic vein. The greatest diagnostic difficulties inhere in differentiating gastric ulcer from liver cirrhosis. Here laboratory confirmations of hepatic insufficiency afford no positive proof of cirrhotic involvement, as the same confirmations may be obtained for ulcer. The Takata-Ara test is always negative in ulcer and often, but not always, positive in biliary cirrhosis. Ultimately, differential diagnosis must rely on purely clinical analyses and morphologic methods of examination, such as the roentgen rays and the various forms of endoscopy. The fact that both pathologic processes are not infrequently found coexistent complicates the situation still further. In gastric hemorrhage due to malignant nephrosclerosis, an increase of nonprotein nitrogen is inconclusive for renal insufficiency as long as blood is present in the digestive tract.

Endometrial Implants in Small Intestine and Navel.—Aronsson reports the case of a woman aged 43 with endometrial implants in the small intestine which were associated with endometrial implants in the navel. The patient was hospitalized for acute intermittent spasmodic pain in the lower part of the abdomen. The history of the case disclosed that for three years a small nodule situated on the umbilicus would swell, become painful and bleed with every onset of the menstrual flow. After roentgenoscopy surgical intervention was done for ileus. The causative agent of ileus was found to be a cicatricial contraction in that portion of the small intestine in which the ileum begins, with a considerable narrowing of the lumen, which suggested cancer. A portion of the intestinal area was resected. Microscopic examination established endometriosis. The patient made an uneventful recovery. Pains no longer occurred at menstruation. However, the umbilical nodule when last seen showed a threatening enlargement and suggested the necessity of extirpation. Endometrial implants are defined by the author as tissue growths presenting the same microscopic picture as the mucosa of the uterus but occurring outside its distinctive domain. Endometrial implants on the surface of the intestine are usually asymptomatic and encountered at operation. Endometrial implants in the ileocecal area are usually diagnosed as chronic appendicitis. Spread by infiltration, they frequently cause stenotic complications and invite the diagnosis of carcinoma. Since it is almost impossible to establish a differential diagnosis from cancer, endometrial implants in the small intestine require operation. Endometrial implants in the navel are likewise very common. The clinical aspect is that of a nodule of relatively large or small size presenting swelling, pain and often bleeding. After the cessation of the menstrual flow, the navel dries and leaves an encrustation. The phenomena recur at the next cycle. The author briefly discusses the kinds of implants, their microscopic structure, their shape and appearance, the procedure of their diffusion, their usually benign evolution and the observations of previous investigations, and presents bibliographic references.

JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE DEPARTMENT, JULY-DECEMBER 1940

Titles have been listed or Abstracts made of important articles in the following journals in the Current Literature Department of THE JOURNAL during the past six months. Any of the journals, except those starred, will be lent by THE JOURNAL to subscribers in continental United States and Canada and to members of the American Medical Association for a period not exceeding three days. Three journals may be borrowed at a time. No journals are available prior to 1931. Requests for periodicals should be addressed to the Library of the American Medical Association and should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Thus most of these journals are accessible to the general practitioner.

Acta chirurgica Scandinavica. Stockholm.
Acta medica Scandinavica. Stockholm.
Acta obstetricia et gynecologica Scandinavica. Stockholm.
Acta ophthalmologica. Copenhagen.
Acta pædiatrica. Stockholm.
Acta radiologica. Stockholm.
American Heart Journal. St. Louis.
American Journal of Cancer. New York.
American Journal of Clinical Pathology. Baltimore.
American Journal of Digestive Diseases. Huntington, Ind.
*American Journal of Diseases of Children. A. M. A., Chicago.
American Journal of Hygiene. Baltimore.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. St. Louis.
American Journal of Orthopsychiatry. Menasha, Wis.
American Journal of Pathology. Boston.
American Journal of Physiology. Baltimore.
American Journal of Psychiatry. New York.
American Journal of Public Health. New York.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Journal of Syphilis, Gonor. and Venereal Diseases. St. Louis.
American Journal of Tropical Medicine. Baltimore.
American Review of Tuberculosis. New York.
Anais brasileiros de ginecologia. Rio de Janeiro.
Anales de la Facultad de medicina de Montevideo.
Anesthesiology. New York.
Annali dell'Istituto "Carlo Forlanini." Rome.
Annali di ottalmologia e clinica oculistica. Genoa.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otology, Rhinology and Laryngology. St. Louis.
Annals of Surgery. Philadelphia.
*Archives of Dermatology and Syphilology. A. M. A., Chicago.
Archives of Disease in Childhood. London.
*Archives of Internal Medicine. A. M. A., Chicago.
*Archives of Neurology and Psychiatry. A. M. A., Chicago.
*Archives of Ophthalmology. A. M. A., Chicago.
*Archives of Otolaryngology. A. M. A., Chicago.
*Archives of Pathology. A. M. A., Chicago.
Archives of Physical Therapy. Chicago.
*Archives of Surgery. A. M. A., Chicago.
Archivio per le scienze mediche. Turin.
Archivos argentinos de pediatría. Buenos Aires.
Archivos de oftalmología de Buenos Aires.
Archivos de pediatría del Uruguay. Montevideo.
Archivos uruguayos de medicina, cirugía y especialidades. Montevideo.
Athena. Rome.
Atti della Società italiana di ostetricia e ginecologia. Rome.
Australian and New Zealand Journal of Surgery. Sydney.
Bibliotek for læger. Copenhagen.
Boletín de la Asociación médica de Puerto Rico. Puerto Rico.
Boletín de la Sociedad cubana de pediatría. Havana.
Brain. London.
Brasil-medico. Rio de Janeiro.
British Heart Journal. London.
British Journal of Children's Diseases. London.
British Journal of Dermatology and Syphilis. London.
British Journal of Experimental Pathology. London.
British Journal of Ophthalmology. London.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Urology. London.
British Medical Journal. London.
Bruxelles-médical. Brussels.
Bulletin of Health Organisation of League of Nations. Geneva.
Bulletin of the Johns Hopkins Hospital. Baltimore.
Bulletin of the New York Academy of Medicine. New York.
California and Western Medicine. San Francisco.
Canadian Medical Association Journal. Montreal.
Canadian Public Health Journal. Toronto.
Chinese Medical Journal. Peiping.
Chirurg. Berlin.
Chirurgia degli organi di movimento. Bologna.
Connecticut State Medical Journal. Hartford.
Delaware State Medical Journal. Wilmington.
Dermatologica. Basel.
Deutsche medizinische Wochenschrift. Leipzig.
Deutsche Zeitschrift für Chirurgie. Berlin.
Deutsche Zeitschrift für Nervenheilkunde. Berlin.
Día médico. Buenos Aires.
East African Medical Journal. Nairobi.
Edinburgh Medical Journal.
Endocrinology. Los Angeles.
Gazzetta degli ospedali e delle cliniche. Milan.
Geneeskundig tijdschrift voor Nederlandsch-Indië. Batavia.
Ginecologia. Turin.
Giornale di clinica medica. Parma.
Giornale italiano di dermatologia e sifiliologia. Milan.
Glasgow Medical Journal.
Helvetica medica acta. Basel.
Illinois Medical Journal. Chicago.
Indian Medical Gazette. Calcutta.
Journal of Allergy. St. Louis.
Journal of the Arkansas Medical Society. Fort Smith.
Journal of Aviation Medicine. St. Paul.
Journal of Bone and Joint Surgery. Boston.
Journal of Clinical Investigation. New York.
Journal of Endocrinology. London.
Journal of Experimental Medicine. New York.
Journal of the Florida Medical Association. Jacksonville.
Journal of Hygiene. London.
Journal of Immunology. Baltimore.
Journal of the Indiana State Medical Association. Indianapolis.
Journal of Industrial Hygiene and Toxicology. Baltimore.
Journal of Infectious Diseases. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of the Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal-Lancet. Minneapolis.
Journal of Laryngology and Otology. London.
Journal of the Maine Medical Association. Portland.
Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal of Mental Science. London.
Journal of the Michigan State Medical Society. Muskegon.
Journal of the Missouri State Medical Association. St. Louis.
Journal of Nervous and Mental Disease. New York.
Journal of Neurology and Psychiatry. London.
Journal of Neurophysiology. Springfield, Ill.
Journal of Nutrition. Philadelphia.
Journal of Obstetrics and Gynaecology of British Empire. Manchester.
Journal of the Oklahoma State Medical Association. Oklahoma City.
Journal of Pathology and Bacteriology. Edinburgh.
Journal of Pediatrics. St. Louis.
Journal of Pharmacology and Experimental Therapeutics. Baltimore.
Journal of the Philippine Medical Association. Manila.
Journal of Physiology. Cambridge
Journal of the South Carolina Medical Association. Greenville.
Journal of the Tennessee State Medical Association. Nashville.
Journal of Thoracic Surgery. St. Louis.
Journal of Urology. Baltimore.
Kentucky Medical Journal. Bowling Green.
Kinderärztliche Praxis. Leipzig.
Klinische Monatsblätter für Augenheilkunde. Stuttgart.
Klinische Wochenschrift. Berlin.
Lancet. London.
Laryngoscope. St. Louis.
Lisboa médica. Lisbon.
Lotta contro la tubercolosi. Rome.
Medical Annals of the District of Columbia. Washington.
Medical Bulletin of the Veterans' Administration. Washington, D. C.
Medical Journal of Australia. Sydney.
Medicina. Mexico City.
Medicine. Baltimore.
Medizinische Klinik. Berlin.
Medizinische Welt. Berlin.
Military Surgeon. Washington, D. C.
Minerva medica. Turin.
Minnesota Medicine. St. Paul.

*Cannot be lent.

Monatsschrift für Kinderheilkunde. Berlin.
Monatsschrift für Ohrenheilkunde. Berlin.
Münchener medizinische Wochenschrift. Munich.
Nebraska State Medical Journal. Lincoln.
Nederlandsch tijdschrift voor geneeskunde. Amsterdam.
Nervenarzt. Berlin.
New England Journal of Medicine. Boston.
New Orleans Medical and Surgical Journal.
New York State Journal of Medicine. New York.
New Zealand Medical Journal. Wellington.
Nordisk medicin. Gothenburg.
North Carolina Medical Journal. Winston-Salem.
Northwest Medicine. Seattle.
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SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "OS," Organization Section; "SS," Student Section; "ab," abstracts; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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SOCIETIES

Acad.—Academy *Med.—Medicine*
Am.—American *Nat.—National*
A.—Association *Phar.—Pharmaceutical*
Coll.—College *Phys.—Physicians*
Conf.—Conference *Rev.—Revision*
Cong.—Congress *Ry.—Railway*
Conv.—Convention *Soc.—Society*
Dist.—District *Surg.—Surgery*
Hosp.—Hospital *Surgs.—Surgeons*
Internat.—International *S.—Surgical*
M.—Medical

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